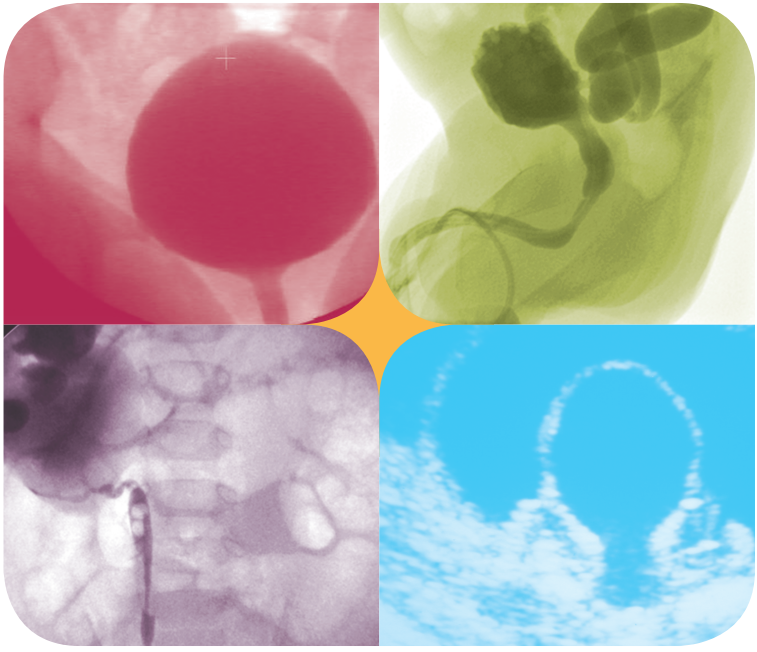
Pediatric Urology

for Primary Care



Editors
Saul P. Greenfield, MD, FAAP, FACS
Christopher S. Cooper, MD, FAAP, FACS

American Academy of Pediatrics
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We dedicate this book to all those who care for children—
it is our sincere hope they find this book useful.

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Introduction

Disorders of the genitourinary system are commonly seen in infants, children, and young adults. In addition, issues of overall genitourinary health are of major concern to parents, schools, and society at large. These issues include socially acceptable urinary continence, renal function, malignancies, and future fertility. As such, pediatric urologists are partners—along with pediatric primary care providers—in the comprehensive care of children of all ages. The intended audience of this book, therefore, includes pediatricians, family practitioners, and allied health professionals.

This *Pediatric Urology for Primary Care* handbook is meant to be a resource to which pediatric primary care providers can turn for practical and contemporary approaches to these disorders. Chapters that deal with the more frequently encountered conditions have been placed earlier in the text. Each chapter has succinct descriptions, with illustrations if appropriate. Clinical pearls are listed for ready reference, and resources for parents and primary care providers are provided at the end of each chapter, including online references. This book can therefore be used by busy clinicians every day and for parent education.

We thank the authors for their hard work and expertise. We are also grateful to the American Academy of Pediatrics and its entire publishing staff for facilitating this endeavor from the outset. Finally, we owe a great deal to Heather Babiar, MS, for her editorial oversight and assistance.

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CHAPTER 1

Urological Emergencies in Pediatrics

Pierre E. Williot, MD, FAAP

Introduction

True urological emergencies in pediatrics—ones that require rapid surgical intervention—are relatively rare. Herein are the most common problems that benefit from urgent urological consultation, either in an emergency department or in the outpatient setting. Urinary tract infection (UTI) and stone disease (lithiasis) are discussed more extensively in Chapter 6, Pediatric Urinary Tract Infection, and Chapter 11, Pediatric Urolithiasis.

The Acute Scrotum

Acute scrotal pain and swelling can result from several possible causes. Those requiring urgent surgical intervention include testicular torsion, traumatic testicular rupture, and incarcerated inguinal hernia and must be differentiated from those that can be observed or treated medically.

Testicular Torsion in the Older Child and Adolescent

History

Testicular torsion—or twisting of the spermatic cord—is characterized by sudden, not gradual, onset of pain. This is different from the much less common neonatal torsion, which is asymptomatic and typically appears at birth with a painless, enlarged, and firm testicle, sometimes without clinically significant scrotal swelling or erythema. Testicular torsion at an older age is often associated with nausea and vomiting, as well as the acute onset of pain. Testicular torsion occurs more frequently in postpubescent adolescents and adults but can happen at any age. It is not caused by any activity or trauma and often occurs while sedentary or even during sleep. There are no voiding symptoms, such as urgency, dysuria, or hematuria. There may be associated lower abdominal or inguinal discomfort, which can mislead the physician. Torsion can also be episodic and followed by spontaneous detorsion, and the child may report several episodes of severe testicular pain that came and went. Undescended testes in the inguinal canal may be predisposed to torsion and may manifest as acute abdomen.

Physical Examination

The scrotum and testes are exquisitely tender and difficult to examine. If the child presents early, usually within 6 hours after the torsion occurs, there will be minimal scrotal erythema or edema. If the child presents later, when the testicle has infarcted, there will be scrotal swelling and redness due to the inflammatory reaction from necrotic tissue (**Figures 1-1** and **1-2**). Pain may be diminished or absent in later stages of the condition, when the testicle is no longer viable and nerve input is, therefore, minimal.

It is important to examine the inguinal canal to exclude a coincident inguinal hernia or an undescended testis with torsion. The pressure from an incarcerated hernia can cause diminished blood supply to the testis, also resulting in infarction. In isolated testicular torsion, the inguinal canal above the scrotum is flat and nontender. The testis may have an abnormal horizontal lie, but this is frequently difficult to determine because of the overall enlargement and swelling of the scrotum.

Figure 1-1. Scrotal appearance in a patient with testicular torsion and infarction, with associated scrotal erythema.

Laboratory Values

There are no diagnostic laboratory tests for testicular torsion. The urinalysis results will be within reference range without evidence of infection.

Diagnosis

Urological consultation to evaluate suspected testicular torsion should be rapid, since the chance of testis survival diminishes with increasing duration of torsion. If the torsion is left untreated for longer than 6 hours, the chance of testicular salvage decreases. Therefore, if the

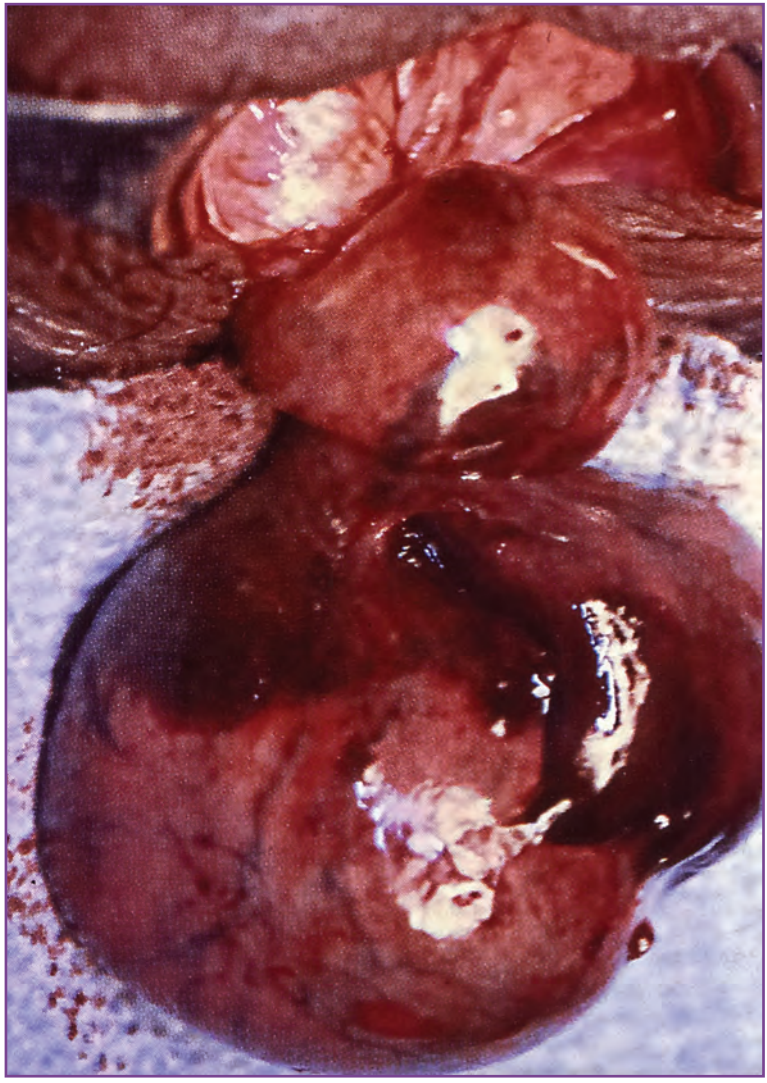

Figure 1-2. A testis with torsion and infarction in an adolescent patient.

history and physical examination findings are consistent with torsion, urological consultation should be obtained immediately, and scrotal ultrasonography (US) should not be performed if it will delay surgical exploration. The role of scrotal US in a child with an acute scrotum is to confirm the clinical suspicion that the patient *does not* have torsion.

If US is performed and demonstrates absence of blood flow, immediate surgical exploration is indicated. There is frequently a reactive hydrocele around a testicular torsion. While not absolutely diagnostic, the cremasteric reflex (stroking the inner thigh, which causes the testes to rise) is often absent. If the diagnosis is uncertain or in doubt, surgical exploration is warranted.

Treatment

It may be possible to achieve manual detorsion of the testis, and this is best done after a nerve block with lidocaine of the spermatic cord is performed. One can never be certain that manual detorsion is adequate, and surgical exploration should follow. Surgery entails correcting the torsion of the affected testis. If the testis is salvageable, both testes should undergo fixation with a suture to prevent future torsion—called *scrotal orchidopexy.* If one testis is infarcted and removed, orchidopexy should be performed on the contralateral testis. While often difficult to confirm, if there is a high degree of suspicion regarding episodes of acute pain that come and go—which might be torsion or detorsion—elective bilateral scrotal fixation should be considered.

Neonatal Torsion

History

Testicular torsion can occur in utero or shortly after birth. The cause is unknown but has been associated with prolonged, difficult labor and neonates who are large for gestational age. Neonates with this form of torsion are asymptomatic and do not appear to be in discomfort. The diagnosis is frequently established after a routine examination reveals a swollen scrotum with induration of the testis. While most often unilateral, torsion can occur in the contralateral testis postnatally, rendering the child anorchic.

Physical Examination

The affected scrotum may be swollen and erythematous, but there may be minimal scrotal skin reaction at times. The testis is firm and hard to palpation. Inguinal hernias are not commonly associated with neonatal torsion but must be excluded.

Figure 1-3. A testis with torsion and infarction in a neonate.

Diagnosis

The physical findings alone may be sufficient. Scrotal US will also demonstrate absence of blood flow. The urinalysis results will be within reference range.

Treatment

Although there is some debate, many urologists believe that urgent surgical exploration is warranted to remove the affected testis and fixate the contralateral side. Salvage of an affected testis in the neonatal period has been reported but is rare. The aim of surgery is to prevent contralateral torsion. The timing of surgery depends on the availability of pediatric anesthesia and whether or not there are any other comorbid conditions that would increase risk. While there is no need for surgery immediately after birth, it is prudent to do so within several days (**Figure 1-3**).

Torsion of the Appendix Testis or Appendix Epididymis

History

Torsion of the testicular appendages is the most common cause of acute scrotum in the prepubescent child. These appendages are müllerian and wolffian ductal remnants located along the upper pole of the testis and epididymis and have no function (**Figure 1-4**).

Figure 1-4. Appendix testis with torsion and infarction along the upper pole of the testis.

The testicular appendages can spontaneously twist, interrupting their blood supply, and result in infarction and inflammation. The resulting pain and swelling can last for up to a week and spontaneously resolve. This does not commonly occur in the postpubescent male. As opposed to testicular torsion, the pain is less severe and more gradual in onset and is *not* associated with acute nausea and vomiting. There are no urinary voiding symptoms. There are no predisposing physical activities or etiologic origins.

Physical Examination

Early on, if the scrotal skin is not affected, one may palpate induration along the upper pole of the testis, which can be localized "point tenderness." There may also be a "blue dot" sign, representing the infracted appendage seen through the thin prepubertal scrotal skin (**Figure 1-5**).

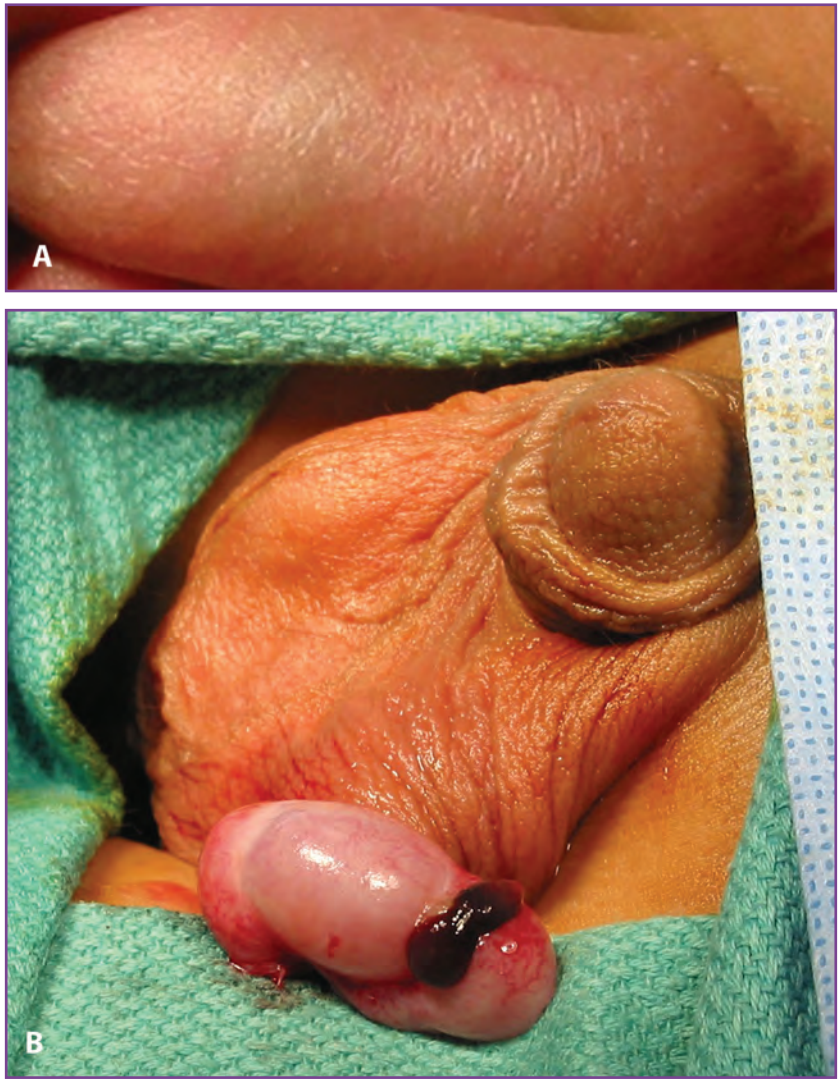

Figure 1-5. A, The "blue dot" is sign is seen through the scrotal skin. **B,** Upon scrotal exploration, the appendix testis with torsion and infarction is confirmed.

Later, after inflammation has progressed, the entire hemiscrotum may be swollen and indurated, and erythematous and testicular landmarks cannot be discerned. A cremasteric reflex is most often present. The urinalysis results will be within reference range. Because the induration involves the upper pole of the epididymis, this is often misdiagnosed as epididymitis. However, a bacterial epididymitis is rare in the prepubescent male patient, especially if there are no voiding symptoms and a normal urinalysis result.

Diagnosis

Early physical findings and history, as described earlier, are diagnostic. Scrotal US can be used to confirm normal blood supply to the testis and inflammation of the upper pole of the epididymis. There may be a reactive hydrocele.

Treatment

The treatment is observation and nonsteroidal anti-inflammatory medication, such as ibuprofen. Antibiotics are not needed. Surgery may be indicated if the symptoms are severe or persistent and is certainly indicated if the diagnosis of testicular torsion is entertained.

Epididymo-orchitis

History

Inflammation and infection of the epididymis and testis are relatively rare in the prepubescent, non–sexually active male patient. Urinary infection, however, as well as rare functional and congenital abnormalities of the lower urinary tract, can predispose the patient to epididymo-orchitis. These abnormalities include posterior urethral valves, neurogenic bladder, and an ectopic ureter to the vas deferens. The male adolescent, with or without admitted sexual exposure, may at first be presumed to have sexually related epididymo-orchitis. The route of infection is retrograde flow of bacteria from the posterior urethra to the epididymis (**Figure 1-6**).

In epididymo-orchitis, the testicular pain is most often gradual in onset. The irritative voiding symptoms of urinary infection (urgency, frequency, and dysuria) may be present. Urethral discharge may be present between voids in the sexually active male patient. Fever and

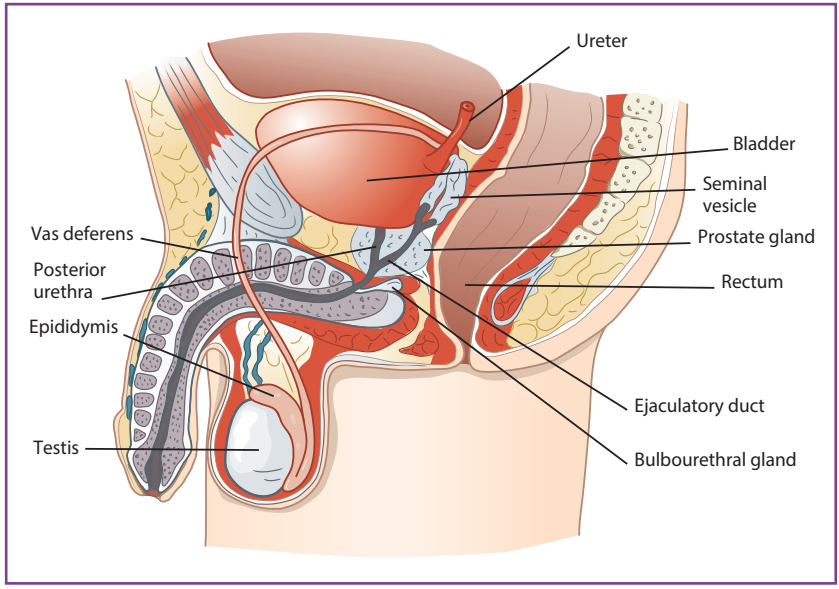

Figure 1-6. Diagram illustrates the anatomic relationship between the epididymis, the vas deferens, and the posterior urethra.

chills can occur. Bacterial infection in the prepubescent, non–sexually active male patient necessitates a thorough anatomic evaluation of the genitourinary tract with renal and bladder US and—at a later date, once the UTI has been treated—voiding cystourethrography.

Physical Examination

During the early stage, an indurated, tender epididymis, either upper or lower pole, may be palpated. Scrotal skin changes will be minimal. The cremasteric reflex may be preserved. Later, the scrotum will be swollen, and erythematous and testicular landmarks will not be palpable. Rectal examination of the postpubescent male patient may also demonstrate a boggy, tender prostate, which is consistent with associated prostatitis.

Diagnosis

A positive urinalysis result, indicating infection, will be present. Scrotal US should demonstrate normal or increased blood flow to the area, with swelling of the epididymis. Reactive hydrocele may be present. Severe orchitis may demonstrate disruption of the normal, homogeneous testicular parenchyma. There can be abscess formation within the testis.

Treatment

A urine specimen must be sent for culture. Sexually active male patients can be treated with antibiotics directed toward *Chlamydia trachomatis* and *Mycoplasma genitalium*, such as doxycycline or azithromycin, respectively. The younger prepubescent boy can be empirically treated with antibacterials directed toward gram-negative bacilli and then switched, once culture and sensitivity are known. Oral antibiotics may suffice for most cases. However, severe cases of fever and increased white blood cell counts might require hospital admission and intravenous antibiotics.

Incarcerated Inguinal Hernia and Acute Hydrocele

The inguinal canal should never be overlooked when evaluating an acutely swollen and inflamed scrotum. Pathologic findings confined to the testis will not be associated with inguinal bulging. Both testicular torsion and an incarcerated inguinal hernia can manifest with nausea and vomiting. A nonreducible inguinal bulge is strongly suggestive of hernia (**Figure 1-7**). This can be corroborated by inguinal and scrotal US, but imaging is most often not needed.

Infants and children are often urgently brought to the emergency department due to the sudden appearance of a swollen scrotum, without erythema or symptoms of pain and tenderness. Communicating hydroceles can become rapidly apparent and just as readily reduce in size or disappear altogether. The scrotal skin is typically normal, and the hydrocele fluid may appear bluish underneath and can be transilluminated. The bulge may extend up into the inguinal canal. Ultrasonography, while most often not necessary, will show the testicle surrounded by fluid. Acute hydroceles or easily reducible inguinal hernias are not an emergency and surgery can be performed electively. Parents should be counseled on the signs and symptoms of an incarcerated or strangulated hernia. Incarcerated hernias require emergent manual reduction, if possible. If reduction is not possible, surgery should be performed urgently.

Henoch-Schönlein Purpura

Henoch-Schönlein purpura can manifest with testicular and scrotal findings. It is most often seen after a nonspecific systemic viral illness. Classically, there are purpura that usually involve at least the lower extremities. There can be an associated testicular vasculitis, with scrotal swelling, mild erythema, and a purple cast to the scrotal skin (**Figure 1-8**).

Figure 1-7. Obvious right inguinal bulge above the scrotum, representing an inguinal hernia.

The process is bilateral, so it is unlikely to be testicular torsion or appendix testis torsion. Testicular US shows normal or enhanced arterial flow bilaterally. There is no specific urological intervention required, and the process most often resolves without testicular sequelae.

Allergic Reaction and Severe Rash

Prepubescent children and infants who wear diapers can present with acute bilateral scrotal erythema, swelling, and scrotal skin thickening (**Figure 1-9**).

Figure 1-8. Characteristic appearance of a dusky, purple hue seen bilaterally with testicular and scrotal involvement of Henoch-Schönlein purpura.

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The etiologic origin can be obscure and may be attributed to reaction from a bug or spider bite or a sensitivity to diaper or laundry products. Severe diaper rash may also have this appearance. The erythema may progress to the suprapubic area or the thighs. Examination findings of the testes are normal, but examination may be difficult because of the overlying edema. Scrotal US can be used to confirm normal testicular morphologic appearance and blood flow. Treatment consists of removal of the offending agent, if identified. Antihistamines are helpful. If

Figure 1-9. Severe diaper rash involving the scrotum and inner thighs.

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cellulitis is suspected, oral broad-spectrum antibiotics—often a cephalosporin—can be administered for several days; however, most diaper rashes are fungal in origin.

Penile Issues

Phimosis, Balanitis, Paraphimosis, Penile Adhesions, and Hair Tourniquet

Phimosis and paraphimosis only occur in boys who have not been circumcised. Phimosis is the inability to easily retract the foreskin. This is normal in most boys younger than 3 years, and parents should be advised that it is not necessary or desirable to try to routinely retract the foreskin during infancy. Routine hygiene with retraction and cleaning can start in the older child. Presuming that circumcision is not desired, a phimotic foreskin can be treated with topical steroid (triamcinolone or betamethasone) and gentle retraction during bathing. The presence of scarring, as evidenced by a white ring at the tip of the foreskin, often means that circumcision will be needed (**Figure 1-10**). Circumcision, a dorsal slit without circumcision, or a preputioplasty—if the family is

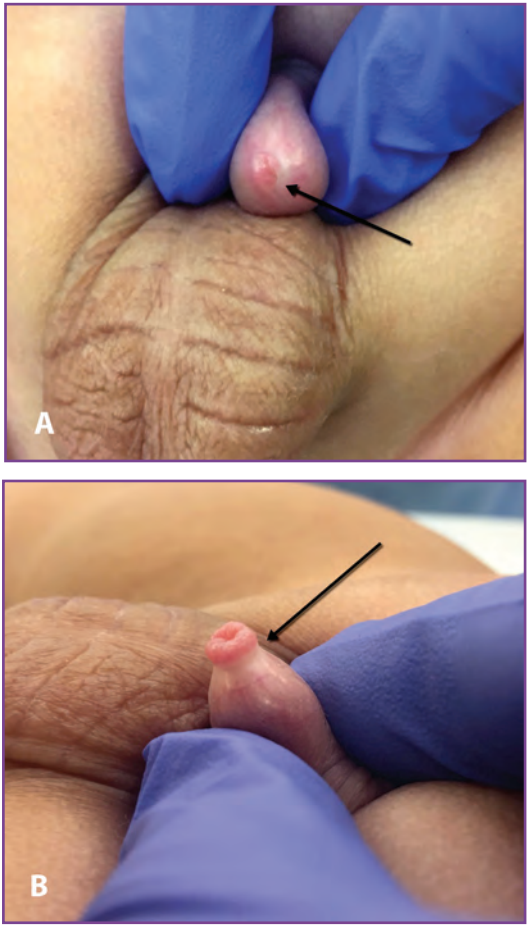


Figure 1-10. Phimotic preputial ring prevents retraction of the foreskin (arrows), seen in (**A**) a head-on view and (**B**) a lateral view. Note the characteristic white ring.

opposed to circumcision—are alternatives if phimosis persists despite topical treatment.

Paraphimosis occurs when the foreskin is retracted and cannot be pulled back over the head of the penis and begins to act like a tourniquet proximal to the head of the penis. This is an emergency, since a ring can develop that constricts the glans (**Figure 1-11**).

The foreskin can be reduced in the outpatient setting, with or without the use of local anesthesia. A procedure with general anesthesia is rarely

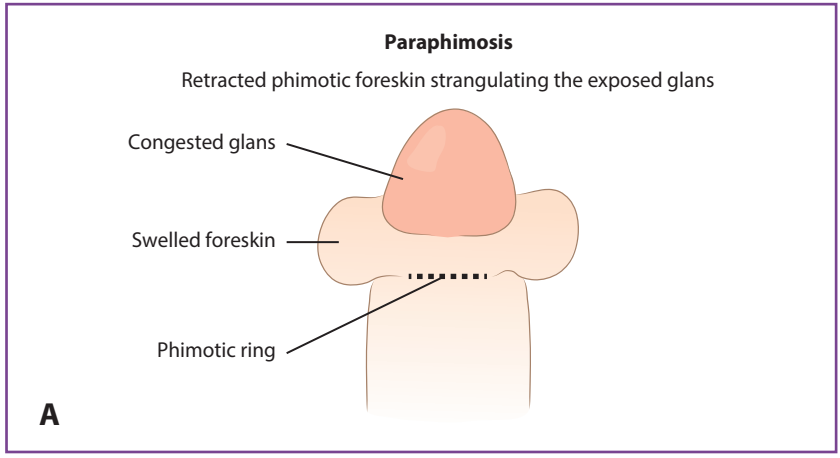


Figure 1-11. A, Diagram demonstrates the appearance of the retracted foreskin in paraphimosis. **B,** The characteristic appearance of paraphimosis is shown.

Image reproduced with permission from Gil Z. Shlamovitz, MD, FACEP, Keck Medicine of USC, published by Medscape Drugs & Diseases (https://emedicine.medscape.com), Paraphimosis Reduction Procedures, 2016, available at https://emedicine.medscape.com/article/143885-overview.

required. Erythema of the foreskin and penile shaft may be present, suggesting infection; after reduction, topical antibiotic ointment and a short course of oral antibiotics may be warranted. Parents and individuals should be warned not to try to retract the foreskin after the initial

episode. An elective circumcision is frequently required at a later date because these foreskins are often inflamed and scarred, making later retraction difficult, if not impossible.

Balanoposthitis is bacterial infection of the glans and foreskin. This appears with erythema and occasional whitish discharge at presentation. There can be more widespread cellulitis involving the penile shaft, scrotum, or lower abdomen. If limited to the foreskin (posthitis), treatment with a broad-spectrum antibiotic—commonly a cephalosporin—for a week suffices. Signs of more widespread cellulitis necessitate intravenous antibiotics. Topical antibiotic ointment can be added. The foreskin should not be retracted. Balanoposthitis tends to recur and can lead to scarring and severe phimosis. Therefore, performing elective circumcision at a later date should be discussed with the family.

Penile adhesions are often seen after neonatal circumcision. They may be epithelialized, making retraction impossible. They can appear emergently, when parents are alarmed at the smegma cysts that can accumulate underneath (**Figure 1-12**). If necessary, treatment of minimal adhesions consists of retraction in the outpatient setting. Pulling back the adhesions, however, is often not necessary or recommended, as it is associated with a higher risk of recurrence and development of epithelialized adhesions. If adhesions are epithelialized and not easily retracted, a brief procedure with general anesthesia will be needed.

Hair tourniquets probably occur during bathing and are seen around toes, as well as the penis. The appearance may be similar to paraphimosis, except these children are most often circumcised. There is an erythematous ring just proximal to the glans. Careful inspection will

Figure 1-12. Characteristic appearance of smegma.

reveal a hair. This is an emergency, since constriction can lead to injury to the glans and transection of the urethra (**Figures 1-13** and **1-14**). Simple cutting and removal of the hair is all that is required.

Figure 1-13. "Decapitation" of the glans penis due to an unrecognized, long-term hair tourniquet.

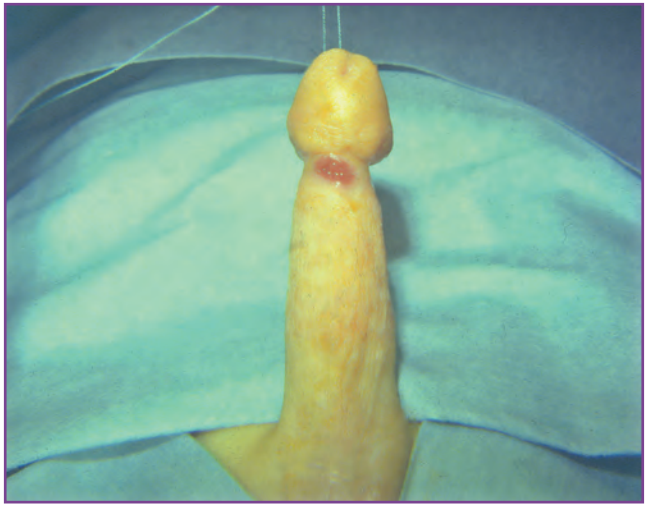


Figure 1-14. Transection of the urethra from an unrecognized, long-term hair tourniquet.

Priapism

Priapism most often occurs in African American patients with sickle cell disease but can occur in others. Hematologic disorders, such as polycythemia or acute leukemia, can also cause priapism. A complete blood cell count should be obtained in all patients without sickle cell disease. The 2 corporal bodies are firm with erection, while the spongy tissue of the glans remains uninvolved. This is an emergency, since recurrent and untreated priapism will lead to fibrosis of the corporal bodies and erectile dysfunction. Medical management of the sickle cell disease should be instituted immediately, which may include analgesia, nasal oxygen, hydration with or without alkalinization, and transfusion. Surgery is required in those who fail to achieve detumescence with medical therapy. Surgical intervention includes irrigation of the corporal bodies and creation of a temporary "shunt" between the 2 corporal bodies and the noninvolved spongy tissue of the glans and urethra. Multiple procedures may be required. Families and individuals should be cautioned that despite therapy, erectile dysfunction may occur.

Gross Hematuria and Urethrorrhagia

Gross hematuria is much less common in children than in adults. Medical causes with a glomerular source should be excluded before referral to a urologist. Urological causes include cystitis, ureteropelvic junction (UPJ) obstruction, renal or ureteral calculi, renal or bladder malignancies, and trauma. Cystitis and documented urinary infection require further urological evaluation (see Chapter 6, Pediatric Urinary Tract Infection). Patients with cystitis have the associated irritative voiding symptoms and may have flank pain from pyelonephritis. Urinary tract calculi and malignancies are more thoroughly discussed in Chapter 11, Pediatric Urolithiasis, and Chapter 12, Urological Oncology in Pediatrics.

UPJ obstruction deserves special mention because gross hematuria and flank pain are often the presenting symptoms. These children can present after minor abdominal or flank trauma. Delicate and stretched vessels, which line the dilated renal pelvis, are easily disrupted and result in gross hematuria. Renal US or computed tomography will show the characteristic hydronephrosis (see Chapter 9, Congenital Hydronephrosis).

By far, the most common pediatric urological referral for "gross hematuria" in boys is not hematuria. In urethrorrhagia, the urine is grossly yellow, but there are spots of blood on the underwear, or drops of blood are seen at the urethral meatus at the end of urination. The history of blood spots in the underwear helps to localize the site of bleeding to the urethra distal to the external sphincter. This is caused by posterior urethritis. No infectious agent is usually identified. At times, there can be a history of trauma between the legs, just behind the scrotum, from bicycle riding, horseback riding, wearing an ill-fitting protective scrotal cup, or doing gymnastics. These activities should be stopped. Most often, no cause can be found. Imaging of the urinary tract is not required, and the symptoms most often resolve after several months. Cystoscopy is also not routinely performed, unless the bleeding persists for more than several months. A characteristic filmy exudate is seen in the posterior urethra.

Urinary Retention

Not including children with obvious neurological disease or those who are taking psychoactive medication, urinary retention in infants and children is rare—especially if the patient had been voiding normally up to the time of presentation. Structural urological anomalies must be excluded with renal and bladder US. Unusual anomalies of the lower urinary tract that can obstruct the bladder outlet include ureteroceles and benign urethral polyps (**Figure 1-15**).

Rarely, an impacted stone can obstruct the male urethra. Bowel habits and constipation should be assessed. Urethral strictures are also rare, except in older boys who may have had recurrent posterior urethritis. Riding a bicycle with a hard seat can cause trauma to the posterior urethra, which might lead to stricture. Physical examination should include inspection of the back to look for cutaneous signs of underlying spinal malformation, such as hair tufts, gluteal asymmetry, sacral sinuses, and discoloration. Anal tone and constipation should be assessed with a rectal examination. Bladder and prostate rhabdomyosarcoma can also appear with voiding symptoms and urinary retention at presentation (see Chapter 12, Urological Oncology in Pediatrics).

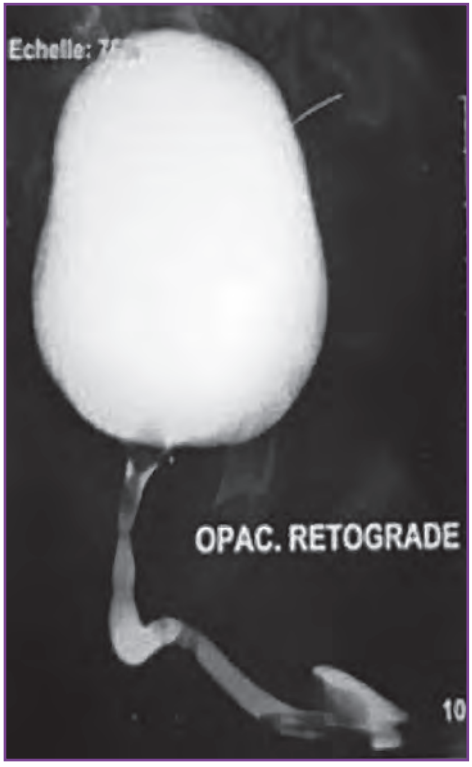


Figure 1-15. Voiding cystourethrogram in a 15-month-old boy shows the radiographic appearance of a benign posterior urethral polyp, just below the bladder neck, which is causing urinary retention.

From Ksia A, Ben saad M, Mekki M, et al. Fibroepithelial polyps of the urethra in infants: a report of three cases. *African J Urol*. 2014;20(1):33.

A Foley catheter can be placed for several days, and intermittent catheterization can be started if the child still cannot void after removal of the catheter. Difficulty in placing a catheter should lead to immediate urological consultation. Assuming that no structural anomaly is found and the urinary symptoms persist, formal urodynamic evaluation should be considered.

When to Refer

All pediatric patients with urological emergencies should be referred to a specialist.

Clinical Pearls

- A testis with torsion has, at most, 6 to 12 hours to survive without atrophy.
- A neonatal testicle with torsion is asymptomatic and rarely salvageable, but surgery should be performed to prevent torsion of the contralateral testis.
- Torsion of the appendix testis is much more common than testicular torsion and does not require surgery. It is often misdiagnosed as epididymitis.
- Epididymitis from infectious causes is rare in preadolescent, non–sexually active individuals; if documented, a complete urological evaluation is needed.
- The inguinal canal should always be inspected in patients with acute scrotal pathologic findings.
- Paraphimosis should be immediately reduced.
- A hair tourniquet can look like paraphimosis, and the hair must be removed immediately.
- Medical causes should be excluded in children with gross hematuria.
- Urinary retention should trigger a complete evaluation for urological and neurological causes.

Resources for Parents

- BMJ Best Practice. Testicular torsion. https://bestpractice.bmj.com/topics/en-us/506. Reviewed September 2018. Accessed October 16, 2018
- BMJ Best Practice. Paraphimosis. https://bestpractice.bmj.com/topics/en-us/765. Reviewed September 2018. Accessed October 16, 2018
- American Urological Association. Management of priapism. https://www.auanet.org/guidelines/priapism-(2003-reviewed-and-validity-confirmed-2010). Reviewed 2010. Accessed October 16, 2018
- BMJ Best Practice. Priapism. https://bestpractice.bmj.com/topics/en-us/505. Reviewed September 2018. Accessed October 16, 2018

References

1. Wein AJ, ed. *Campbell-Walsh Urology.* 11th ed. St Louis, MO: Elsevier Health Sciences; 2015
2. Docimo SG, ed. *The Kelalis-King-Belman Textbook of Clinical Pediatric Urology.* 5th ed. London, United Kingdom: Informa Healthcare UK Ltd; 2007
3. Tanagho EA, McAninch JW, eds. *Smith's General Urology (LANGE Clinical Science).* 16th ed. New York, NY: McGraw-Hill; 2004
4. Belman AB, King LR, Kramer SA, eds. *Clinical Pediatric Urology.* 4th ed. London, United Kingdom: Martin Dunitz Ltd; 2001

CHAPTER 2

Penile Problems, Anomalies, and Procedures

Michelle Lightfoot, MD, and Andrew Kirsch, MD, FAAP, FACS

Phimosis and Paraphimosis

Phimosis is the inability to fully retract the foreskin of an uncircumcised boy due to a constricting band of tissue (the phimotic ring). *Physiological phimosis* is a normal finding in nearly all infant boys and is associated with adhesions between the inner prepuce and the glans penis. As the child grows, sloughed epithelial cells and glandular secretions form *smegma,* which collects under the inner preputial skin and aids in separation of the adhesions (**Figure 2-1**). By age 5, 90% of uncircumcised boys have a fully retractable foreskin, and this figure rises to 99% by puberty.

In a child without clinical sequelae, physiological phimosis may be safely observed without intervention. However, medical or surgical intervention may be considered for boys with prolonged physiological phimosis (**Figure 2-2**). The application of a steroid cream—most commonly 0.05% betamethasone ointment—to the preputial ring twice daily for 4 to 8 weeks results in resolution of phimosis in approximately 85% of boys. This has been shown to be a clinically effective and cost-effective alternative to circumcision. Surgical intervention for phimosis consists primarily of circumcision. Phimosis may be present

Figure 2-1. Normal preputial adhesions with underlying smegma, seen as the white material. No treatment is necessary, but smegma should be gently cleansed away when it becomes exposed.

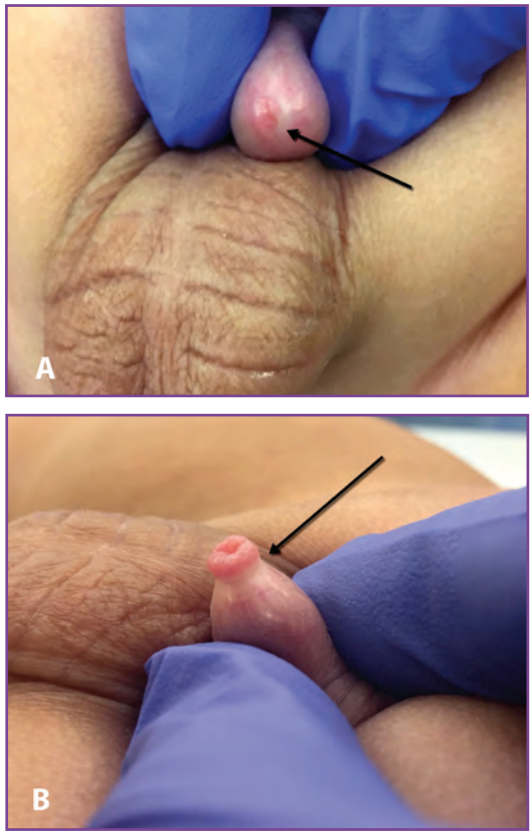


Figure 2-2. Phimotic preputial ring prevents retraction of the foreskin (arrows), seen in (**A**) a head-on view and (**B**) a lateral view. Note the characteristic white ring.

in circumcised boys who have undergone incomplete circumcision or who have obesity or a prominent pubic fat pad. This may lead to a trapped penis, requiring revision circumcision to correct. Preputioplasty, consisting of relaxing incisions in the phimotic band, has been reported but is not commonly performed in the United States.

Pathologic phimosis is defined as an inability to retract the foreskin after puberty or in a previously retractable foreskin. At examination, preputial scarring may be present; this is typically seen as a flat white cicatrix on the foreskin. Lichen sclerosus (also known as *balanitis xerotica obliterans* [BXO]) is a chronic inflammatory condition involving the glans and foreskin, with an estimated prevalence of less than 1%. This may lead to fibrosis of the skin, meatal stenosis, and urethral strictures in later stages of the disease, if untreated. The etiologic origin of lichen sclerosus is unclear, but this is found almost exclusively in uncircumcised men. Although the prevalence has been estimated at 1 in 300 to 1,000 men, some studies indicate that this condition may be underreported. Patients should be followed up regularly to detect and prevent morbidity from long-term complications. Pathologic phimosis secondary to lichen sclerosus and recurrent balanoposthitis that is unresponsive to topical steroids are generally considered the only absolute medical indications for circumcision.

Pathologic phimosis is the most common medical indication for male adults undergoing circumcision. Phimosis may also be associated with dyspareunia, balanoposthitis, poor penile hygiene, and penile cancer in the adult population. Secondary phimosis—acquired unretractability of the foreskin after previously normal function—is more common in men with diabetes and has been reported as the initial manifestation of uncontrolled diabetes. With the growing incidence of diabetes, obesity, and metabolic syndrome in both adults and children, there may be a corresponding increase in the incidence of pathologic phimosis in the future.

Paraphimosis is seen exclusively in uncircumcised or incompletely circumcised boys, typically those with a phimotic band. This occurs when the foreskin is retracted and becomes entrapped behind the glans penis (**Figure 2-3**). Edema of the foreskin and glans results within several hours and may lead to tissue necrosis if left untreated. Treatment primarily consists of manual reduction, although dorsal slit

Figure 2-3. Paraphimosis with edema of the entrapped foreskin.

or circumcision may occasionally be necessary. Various strategies for reduction of paraphimosis have been reported, including manual compression of the glans and edematous foreskin, application of an iced glove for 5 minutes, or multiple punctures of edematous foreskin. The phimotic band should be manipulated until it is located completely distal to the glans. Placement of topical lidocaine and prilocaine cream for 30 to 45 minutes improves tolerability of manual reduction. If a paraphimosis cannot be fully reduced in the clinic, the child should be sent to the emergency department for treatment.

Balanitis

Inflammation of the glans penis and foreskin are referred to as *balanitis* and *posthitis,* respectively (**Figure 2-4**). These may be caused by trauma, mechanical or chemical irritation, sexually transmitted infections (STIs), or nonspecific skin infections. History and physical examination may elucidate the cause and suggest the treatment of balanoposthitis. Poor penile hygiene with accumulated debris under the foreskin is treated with regular cleansing. If phimosis is also present, treatment with a steroid cream for 4 to 8 weeks should be instituted. New household exposures, such as soaps, detergents, or bubble baths, may suggest a chemical irritation that often resolves with discontinuation of the

Figure 2-4. Balanoposthitis with edema and erythema of the foreskin and glans penis.

offending agent. Uncontrolled diabetes or recent antibiotic use may suggest possible candidal involvement, although candidal balanitis is rare in children. A short course of an antifungal cream, such as clotrimazole, may be prescribed in such cases. Infection with *Streptococcus pyogenes* is often associated with a thin, purulent discharge under the inner prepuce, local erythema and pain, and a moist transudate or exudate on the glans surface. A rapid antigen test and/or culture swab should be performed if streptococcal balanitis is suspected, and a standard antistreptococcal course of antibiotics is prescribed. In sexually active boys (or those in whom sexual abuse is suspected), infectious etiologic origins, such as chlamydia and gonorrhea, must be considered—especially if urethral discharge is present. Appropriate laboratory testing and antibiotic treatment should be implemented.

For other nonspecific cases of balanoposthitis, treatment consists of regular sitz baths, cleansing of the glans and inner prepuce, bacitracin ointment, and steroid cream. Phimosis may be either a cause or an effect of recurrent balanoposthitis. If this does not respond to treatment with steroid cream, or if scarring or lichen sclerosus are suspected, the patient should be referred for circumcision.

Meatal Stenosis and Meatitis

Meatal stenosis, a narrowing of the urethral meatus, has been reported in 5% to 20% of circumcised boys, depending on the study population and the definition used. The exact rate of meatal stenosis that requires surgical intervention is not known but is likely around 1%. In addition, meatal stenosis may occur in boys with uncorrected hypospadias or as a postoperative complication after hypospadias repair (1%–2%). There are several theories about the etiologic origins of meatal stenosis after circumcision, including chemical and mechanical irritation of the meatus (eg, as the glans is exposed to wet diapers) and meatal ischemia from division of the frenular artery during circumcision. Although many boys may have a urethral meatus that visually appears to be small, surgical correction is typically reserved for those who are symptomatic. Patients or parents may report that the boy has an upward deflected urinary stream or must direct the penis downward to void into the toilet. Other symptoms include penile pain at the beginning of voiding or a narrow, high-velocity urinary stream. More serious conditions related to meatal stenosis, such as incomplete emptying with high bladder pressures and secondary vesicoureteral reflux, are extraordinarily rare. Meatal stenosis is not a cause of common urinary complaints, such as urinary incontinence, urgency, or frequency.

Treatment of meatal stenosis may be performed with local anesthetic in the office or with general anesthesia as an outpatient surgery, depending on provider and patient or family preference. If performed in the office, topical lidocaine and prilocaine cream is applied to the glans penis for 30 to 45 minutes. The meatus is clamped ventrally for hemostasis and sharply divided. In the operating room, the urethral mucosa may be advanced to the glans skin with fine, absorbable sutures after the ventral meatal incision is performed. After the procedure, the family is instructed to gently open the meatus and apply antibiotic ointment during diaper changes for 1 to 2 weeks to prevent restenosis (**Figure 2-5**). Occasionally, a meatal dilator may be needed short term.

Meatal stenosis should be distinguished from meatitis, an inflammatory condition of the urethral meatus. Dysuria and erythema with or without a deflected urinary stream are notable in meatitis and are usually absent in meatal stenosis. While both conditions may coexist, meatitis is typically a nonsurgical condition that responds well to antibiotic ointment.

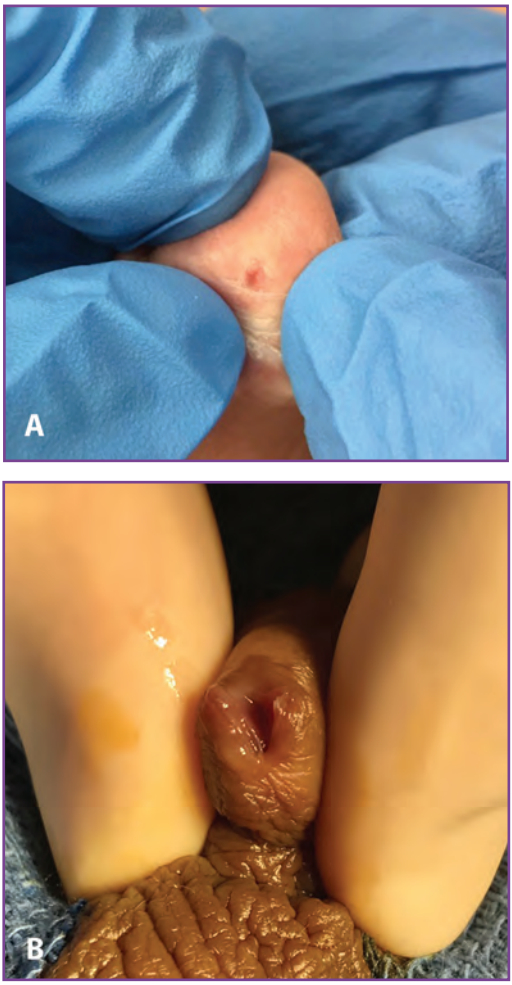


Figure 2-5. **A,** Severe meatal stenosis in a boy who had previously undergone hypospadias repair. **B,** Immediate postoperative appearance after meatotomy.

A short course of antibiotic ointment should be given prior to any surgical intervention if the diagnosis is unclear.

Concealed Penis

A concealed penis—also known as buried, hidden, or retrusive—is normal in size but is hidden in the suprapubic fat pad. This is typically

the result of poor penopubic fixation of the skin at the base of the penis (congenital, **Figure 2-6A** and **2-6B**), obesity (acquired), or scarring after circumcision, with resultant phimotic ring (acquired, **Figure 2-6C** and **2-6D**). Clinically significant scrotal pathologic findings, such as large hydroceles or hernias, may also distort the scrotal anatomy, making the penis appear hidden. Typically, no treatment is needed for congenital and obesity-related concealed penis. However, if circumcision is desired, this should be performed in a surgical setting. A trapped penis

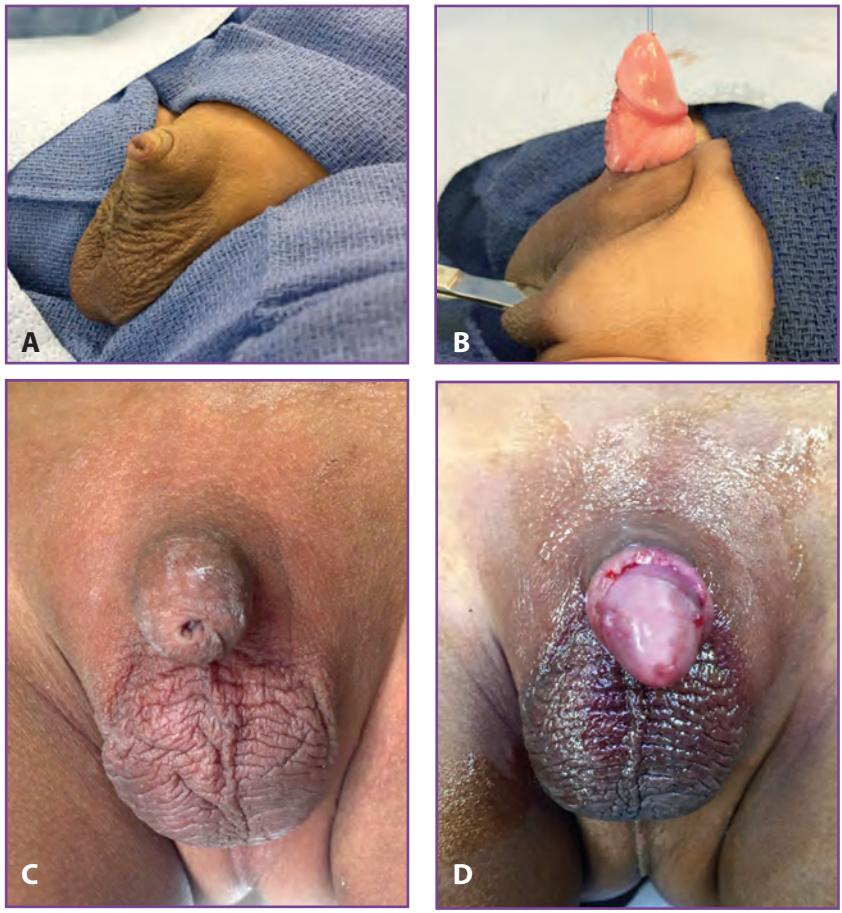


Figure 2-6. A, Congenital concealed (buried) penis. **B,** Appearance after circumcision. Due to the lack of outer shaft skin, most of the penis is covered by inner preputial skin. **C,** Trapped penis after previous circumcision. **D,** Appearance after circumcision revision with excision of the phimotic band

due to post-circumcision scarring may be treated with steroid cream or circumcision revision. Good postoperative care is key in the prevention of complications such as penile adhesions, skin bridges, or recurrence of trapped penis. Specifically, the parents or child must push back the pubic fat pad several times per day to fully expose the penis. Antibiotic ointment should be applied until the circumcision is completely healed.

Penile Bands and Adhesions

Penile bands and adhesions may both be seen after circumcision. Penile bands are skin bridges that connect the penile shaft skin to the glans. This is typically seen when the parents do not regularly expose the penis after circumcision, allowing the circumcision line to heal to the head of the penis. Penile skin bridges will not separate on their own and require surgical intervention (**Figure 2-7**). This may be performed in the office by using topical lidocaine and prilocaine cream for local anesthesia or in the operating room, depending on patient, family, and provider preference, as well as the size, number, and quality of the bands. An office procedure is best suited for single, thin penile bands, whereas thicker or multiple bands should be separated in the operating room. A hemostat

Figure 2-7. A single, thin penile band. This may be divided in the office with local anesthetic if the child and family are calm and cooperative; however, if there is patient or parent anxiety about the procedure, a brief, general anesthetic given in the operating room is more appropriate.

is passed under the band adjacent to the glans tissue, and the tissue is clamped and divided with scissors. If there is a substantial amount of redundant penile tissue after division of the penile bands, a formal circumcision revision may be performed, but it is seldom required. Postoperatively, antibiotic ointment is applied until the tissue is well healed, and the penis should be exposed regularly to prevent recurrence of the skin bridges. After division of thick or multiple bands, the insertion sites on the glans may become edematous, with fibrinous exudate and scabbing for 2 to 3 weeks after the procedure.

In contrast with penile bands, preputial adhesions after circumcision may be a result of a lack of full separation of the physiological adhesions during a newborn circumcision. These may also result from repeat adhesion related to not regularly exposing the glans penis during the postoperative period. As with physiological preputial adhesions, these typically separate over time, without intervention. Administering a course of steroid cream or performing manual separation with local anesthetic in the office may be considered for adhesions that do not resolve by the time of puberty.

Hypospadias

Hypospadias is a congenital disorder of the penis in which the urethral meatus is not located in its normal position on the glans and is located further proximal along the ventral surface (undersurface) of the glans or penile shaft. This is commonly associated with curvature of the penis (chordee) and a hooded prepuce, although boys with mild or distal hypospadias may have a normal foreskin and no chordee. Hypospadias is a common disorder, occurring in approximately 1 in 300 boys. Although most cases are isolated findings rather than a syndromic component, there is a 13-times greater risk in boys who have first-degree relatives with hypospadias. If an infant with hypospadias also has unilateral or bilateral undescended testicles, a disorder of sex development should be considered. In this situation, a karyotype should be obtained, and the child should be referred to endocrinology for further evaluation.

At physical examination, most boys with hypospadias have a dorsal hooded foreskin with absence of foreskin on the ventral shaft. Although there may appear to be a pit or indentation in the glans at the normal

orthotopic location, the true urinary meatus is always the most proximal opening visualized (**Figure 2-8A**). If a child has a known hypospadias, a circumcision should not be performed. However, if the prepuce is normal and a mild variant of hypospadias is discovered incidentally during circumcision, the procedure should be completed as planned. The prepuce is not needed to repair such cases (**Figure 2-8B**).

The goals of hypospadias repair are 3-fold: correct chordee to allow normal sexual functioning, advance the meatus to an orthotopic or near-orthotopic position to allow upright voiding, and obtain a satisfactory cosmetic outcome. Mild phenotypes of hypospadias may not require surgical correction if these goals are met.

For most patients with hypospadias who undergo surgical correction, this is ideally performed before 18 months of age. Numerous surgical techniques for hypospadias repair have been reported, and the specific technique used depends on the severity of hypospadias, associated genital findings (eg, chordee, penoscrotal transposition), and surgeon preference. In general, more severe forms of hypospadias are more likely to be treated with a staged operation and have a higher risk of postoperative complications.

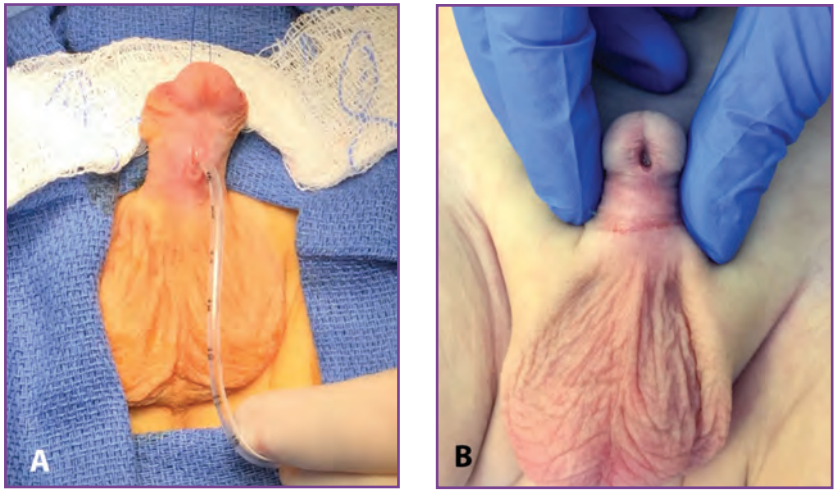


Figure 2-8. A, Midshaft hypospadias with dorsal hooded foreskin. **B,** Mild glanular hypospadias detected after circumcision.

Complications after hypospadias repair include urethrocutaneous fistula, glans dehiscence, meatal stenosis, urethral diverticulum, and recurrent chordee. Of these, urethrocutaneous fistula is the most common. Although some fistulae are large and easily visible, others may not be discovered until the child starts standing to void during toilet training. The patient or his parents may report that the urine mostly comes out the orthotopic meatus but that there is a second stream on the underside of the penis. Patients with proximal hypospadias (proximal shaft, penoscrotal, or perineal) have the highest rates of postoperative complications, with rates of approximately 50% reported in series with long-term follow-up. In contrast, most distal hypospadias repairs are associated with a less than 10% complication rate. Although most complications (80%) manifest within the first year after surgery, others may not be visible until years later. If a child who has previously undergone hypospadias repair is noted or suspected to have a urethral fistula or other complication, he should be referred to a pediatric urologist.

Long-term functional and cosmetic outcomes after hypospadias repair were analyzed in a 2011 review article. When compared with control subjects, men with a history of hypospadias repair were more likely to report urinary symptoms (spraying, deviated stream), weak ejaculations (patients with severe hypospadias), and lower urinary flow rates. Although frequency of intercourse did not differ, patients with hypospadias were less satisfied with their sexual function (81% vs 93% of control subjects) and less satisfied with the penile appearance (46% of patients after proximal hypospadias repairs, 71% of patients after distal hypospadias repairs, and 96% of control subjects). However, several of the techniques used at least 20 years ago for these patients with hypospadias are no longer in widespread use. Long-term data for common urethroplasty techniques used today (eg, the tubularized incised plate, or "TIP") are not yet available, and further studies are needed to determine outcomes in adulthood.

Occasionally, conditions commonly associated with hypospadias may occur as isolated findings (eg, chordee, hooded foreskin, penoscrotal transposition), as seen in **Figure 2-9**. In addition, although the meatus may appear to be in a normal glanular position, the urethra may be thin and fused to the ventral penile skin. This urethral configuration may require formal hypospadias repair for correction. In these situations, neonatal circumcision should not be performed because of the risk of

Figure 2-9. Dorsal hooded foreskin and ventral chordee without associated hypospadias.

creating a urethral fistula, and the child should be referred to a pediatric urologist for surgical care.

Circumcision

Epidemiology

Circumcision is one of the world's oldest, most common, and most controversial procedures. Approximately 35% to 39% of men are circumcised worldwide, although there is significant variability by country, religion, and ethnic group. Approximately two-thirds of circumcisions are performed for religious reasons, primarily among Muslims and Jews (in whom circumcision is nearly universal). The prevalence of circumcision is depicted in **Figure 2-10**, with more than 80% of men in many Middle Eastern and African countries being circumcised and less than 20% in Central and South America, Europe, and southeast Asia. In the United States, circumcision rates peaked at 80% to 85% in the 1960s and 1970s and have slowly declined to current estimates of around 75%. Approximately 57% of newborn males are circumcised before discharge from the hospital, with the remainder undergoing circumcision in other settings (office based or surgical) or remaining uncircumcised. This varies by household income (with a higher circumcision prevalence in households above poverty level), insurance status (with a higher circumcision prevalence with private insurance), ethnicity

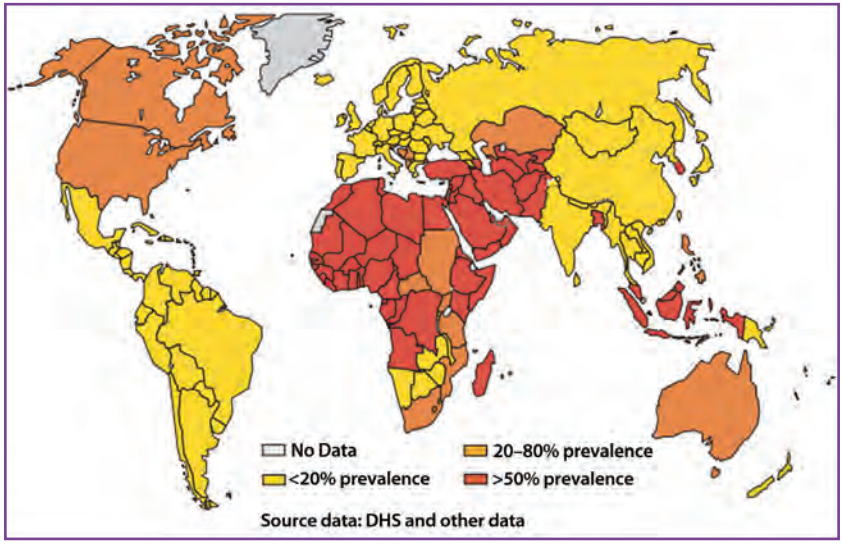


Figure 2-10. Global map of male circumcision prevalence at country level, as of December 2006.

Reprinted with permission from World Health Organization Department of Reproductive Health and Research, Joint United Nations Programme on HIV/AIDS. *Male Circumcision: Global Trends and Determinants of Prevalence, Safety and Acceptability.* Geneva, Switzerland: World Health Organization; 2007. http://apps.who.int/iris/bitstream/10665/43749/1/9789241596169_eng.pdf. Accessed October 16, 2018.

(85% of white men, 80% of black men, and 43% of Mexican American men are circumcised), hospital location (highest prevalence in the Midwest and lowest prevalence in the West), and religious affiliation.

American Academy of Pediatrics Policy Statement

In 2012, the American Academy of Pediatrics (AAP) released its most recent policy statement and technical report on circumcision. The statement endorses the health benefits of newborn male circumcision, including a reduction in the risk of urinary tract infections (UTIs) in the first year after birth, reduction in the heterosexual transmission of HIV and other STIs, and reduction in the risk of penile cancer. The AAP task force concluded that although the health benefits of newborn circumcision outweigh the risks, they are not sufficiently strong to recommend universal adoption of this procedure. The decision for or against circumcision should be made in the context of religious, cultural, and personal preferences for each individual family.

In surveys of American parents, 3 of the most common reasons for desiring circumcision for their sons were improved cleanliness and hygiene of the penis, social reasons (wanting the child to look the same as his circumcised brothers and/or father), and religious reasons. Although penile hygiene is not difficult to perform for an uncircumcised boy, it does require more care than a circumcised penis and must be performed regularly throughout the child's life. Briefly, the foreskin should be gently (not forcibly) retracted after the newborn preputial adhesions have separated, and the entire penis should be cleansed with soap and water. The foreskin should then be pulled forward over the head of the penis again. Although not specifically studied, the ability of the child to eventually perform penile self-care may be a consideration in the decision to circumcise or not. Uncircumcised males with poor penile hygiene are at higher risk of developing infectious complications, such as balanitis and UTIs, as well as penile cancer.

Circumcision and Urinary Tract Infections

UTIs in male patients occur most commonly in the first year after birth. Multiple observational studies have consistently shown a decrease in the rate of UTIs among circumcised boys when compared with uncircumcised boys, with a 3- to 10-fold decrease in boys younger than 2 years. Uropathogens are commonly found in the periurethral area and under the foreskin of uncircumcised boys, and these are more likely to adhere to and colonize the inner mucosal fold of the foreskin than keratinized skin. Periurethral bacterial colonization typically decreases after the first 6 months after birth, which is consistent with the higher prevalence of UTIs in this age group.

Despite a significant relative reduction in UTI risk, the absolute UTI risk in boys is low, regardless of circumcision status. It is estimated that 0.7% to 1.4% of uncircumcised male infants and 0.1% to 0.2% of circumcised infants will develop a UTI in the first year after birth; other studies have estimated that 100 boys would need to be circumcised to prevent 1 UTI. Certain boys, including those with certain urinary tract abnormalities such as vesicoureteral reflux or those with underlying renal disease (in whom pyelonephritis episodes and renal scarring may significantly affect renal function), may derive greater benefit from circumcision than the general population. However, alternate treatment strategies, such as continuous antibiotic prophylaxis or earlier surgical

correction of reflux, may successfully reduce UTI risk for families who prefer that their boys remain uncircumcised.

Circumcision and Sexually Transmitted Infections

Three landmark randomized controlled trials regarding the effect of elective adult circumcision on HIV transmission were published between 2005 and 2007 (from South Africa, Uganda, and Kenya). All trials demonstrated a 40% to 60% lower rate of new HIV infections in heterosexual men who underwent circumcision. In areas with high HIV prevalence and transmission through heterosexual intercourse, widespread circumcision has been advocated as a public health measure to reduce the transmission of HIV. In the United States, most new HIV infections (61%) occur in men who have sex with men. In this population, circumcision has not been conclusively shown to reduce HIV transmission rates. Women account for 23% of new HIV infections in the United States, primarily through heterosexual sex or injection drug use. Although the Ugandan randomized controlled trial reported a lower HIV acquisition rate in women whose male partner was circumcised than in partners of uncircumcised men, other studies have not shown a consistent benefit to the female partner from male circumcision.

Human papillomavirus (HPV) is the most common STI in the United States, with almost all sexually active adults exposed at some point in their lives. Oncogenic strains of HPV cause most cervical, anal, vaginal, vulvar, and penile cancers, while nononcogenic strains cause genital warts. Clinical sequelae of HPV may not manifest until years or decades after infection. Prevalence studies have shown that circumcised men have a 30% to 40% lower likelihood of being infected with HPV, and circumcision also affects the male-to-female risk of HPV transmission. In the Ugandan circumcision trial, female partners of HIV-negative circumcised men had a 23% lower incidence of high-risk (oncogenic) HPV over the study period than corresponding partners of uncircumcised men. However, circumcision did not protect against HPV infection in HIV-positive men. With the relatively recent development of HPV vaccines, it is unclear whether circumcision will have as strong an effect on HPV rates in the future.

There are several potential mechanisms by which circumcision reduces transmission of HIV and other STIs. First, the thin inner foreskin may

be more susceptible to abrasions and micro-tears during sexual activity, which provides an easier entry point for viruses and other pathogens. Second, even without mechanical violation of the epithelium, secretions may get trapped under the foreskin and increase the survival and replication of pathogens. The highly keratinized surface of the circumcised penis may provide a more significant physical barrier to various infections. In addition, the foreskin contains a high density of HIV target cells, such as CD4 T cells, Langerhans cells, and macrophages, which facilitate infection with HIV. Finally, the presence of genital ulcerative diseases, such as herpes simplex virus 2 (HSV-2), increases the coinfection rate with HIV; HSV-2 is more common in uncircumcised men.

Circumcision and Penile Cancer

Squamous cell carcinoma of the penis is rare, with an incidence of 0.58 per 100,000 men between 1993 and 2002 on the basis of the Surveillance, Epidemiology, and End Results (SEER) database. Rates of invasive disease have declined in recent decades, in both the United States (where circumcision is common) and Denmark (where circumcision is rare). In case-control studies, uncircumcised men are at higher risk for developing invasive penile cancer (odds ratio [OR], 2.3 [95% confidence interval, 1.3–4.1]), although no effect was seen for noninvasive carcinoma in situ. However, the presence of phimosis appears to be the more significant risk factor in the development of invasive penile cancer, with an OR of 11.4. In fact, uncircumcised men without phimosis had a decreased risk of invasive penile cancer (OR, 0.5). Estimates of circumcision as prophylaxis against penile cancer are difficult to obtain, with various studies indicating that between 909 and 322,000 newborn circumcisions would be needed to prevent 1 case of penile cancer per year. Improvement in penile hygiene and vaccination against oncogenic HPV are likely to contribute to future declines in penile cancer rates.

Sexual Satisfaction

Proponents and critics of circumcision have long argued about the effects of circumcision on sexual functioning. In the Ugandan HIV trial, men reported less pain with intercourse after undergoing circumcision. Sexual satisfaction remained high in both groups. In a Korean cross-sectional study, adult circumcision was associated with a decrease in pleasure with masturbation. However, multiple other trials have shown

no difference in sexual sensation, orgasm, or satisfaction on the basis of circumcision status.

Procedure, Postoperative Care, and Complications

Neonatal circumcision is performed by using 1 of 3 common devices: the Gomco clamp, Plastibell, or Mogen clamp (**Figures 2-11, 2-12,** and **2-13**). Local anesthesia is administered as either a dorsal penile nerve block or a subcutaneous ring block with 1% plain lidocaine (other local anesthetics, such as bupivacaine, may also be used). Other maneuvers, such as swaddling or use of oral sucrose, may be used as adjunctive calming measures during the procedure but are insufficient to use as sole anesthetics. Topical 4% lidocaine and topical lidocaine and prilocaine cream have also been used as analgesics during newborn circumcision; however, these agents may cause swelling, erythema, and blistering of the skin in 8% to 14% of infants (with higher rates in infants with low birth weight) and are less effective than penile nerve block or ring block.

Recently, a checklist has been developed for assessing suitability for neonatal clamp circumcision (**Figure 2-14**). Within a cohort of newborns referred to pediatric urology clinics for circumcision, 67% were deemed suitable for clamp circumcision. No postprocedural complications were seen. The most common contraindications to newborn circumcision were penile torsion, chordee, and penoscrotal webbing. It is hypothesized that a much higher percentage of newborns in the general pediatric population would be suitable for newborn circumcision by using this checklist.

Although there are slight differences in the use of and outcomes after neonatal circumcision with each device, the Gomco clamp, Plastibell, and Mogen clamp rely on the same general procedural steps. First, the amount of external skin to be removed is estimated. Next, the prepuce is dilated so that the glans is visualized; a dorsal slit may be necessary. The inner prepuce is then bluntly dissected from the glans epithelium, and the device is placed. Hemostasis is achieved by crushing the foreskin, which is then sharply removed. With the Plastibell, a plastic ring is secured with a suture around the 2 edges of the foreskin. The ring typically falls off within 5 to 7 days as the skin sloughs. On occasion, a retained Plastibell ring must be removed by cutting the suture if it has not fallen off by 10 to 14 days after the circumcision.

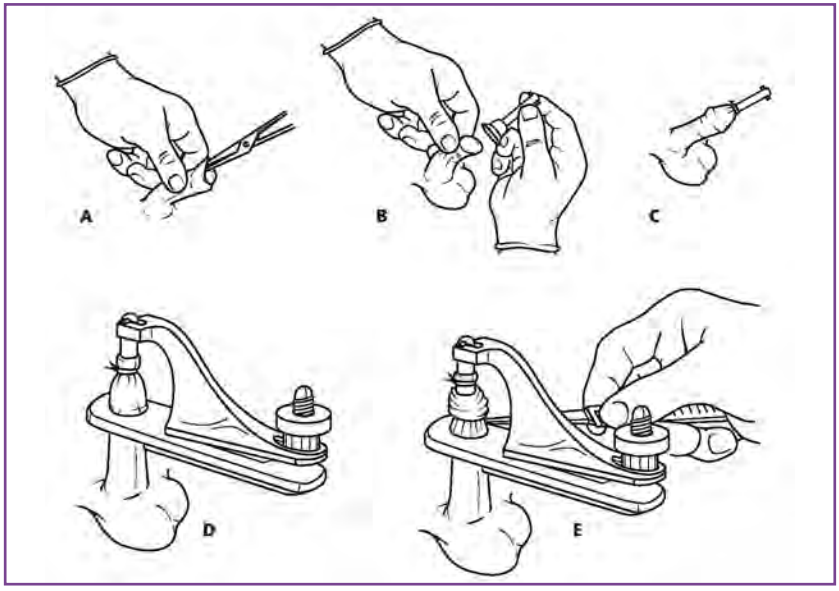


Figure 2-11. The Gomco clamp.

Reprinted with permission from Cornell T, Schmidt JP, Custer JR. Appendix B: outpatient procedures. In: McInerny TK, Adam HM, Campbell DE, DeWitt TG, Foy JM, Kamat DK, eds. *American Academy of Pediatrics Textbook of Pediatric Care.* 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2017:3043.

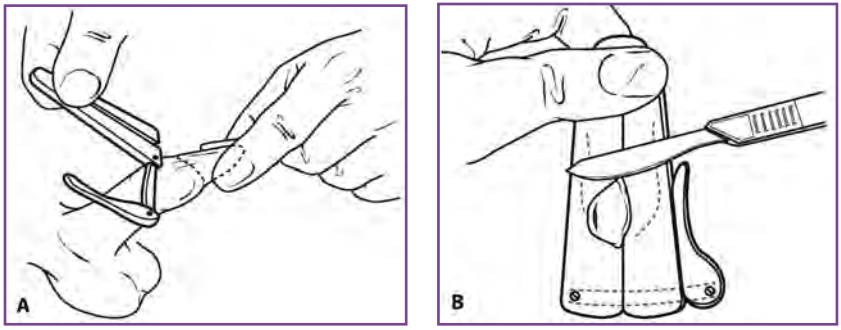


Figure 2-12. The Mogen clamp. **A,** Position the Mogen clamp around the foreskin with the grooved surface facing the glans and lift upward. **B,** While the clamp is closed, using a scalpel, incise the foreskin distal to the clamp.

Reprinted with permission from Cornell T, Schmidt JP, Custer JR. Appendix B: outpatient procedures. In: McInerny TK, Adam HM, Campbell DE, DeWitt TG, Foy JM, Kamat DK, eds. *American Academy of Pediatrics Textbook of Pediatric Care.* 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2017:3044.

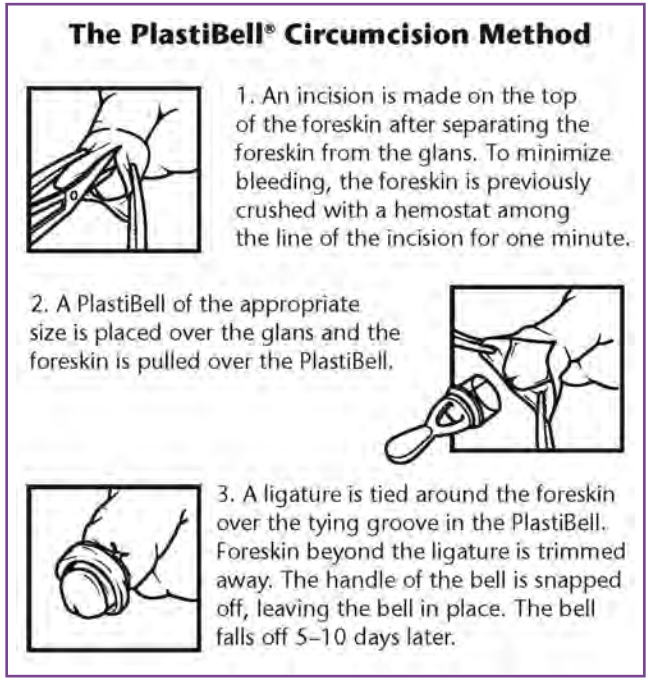
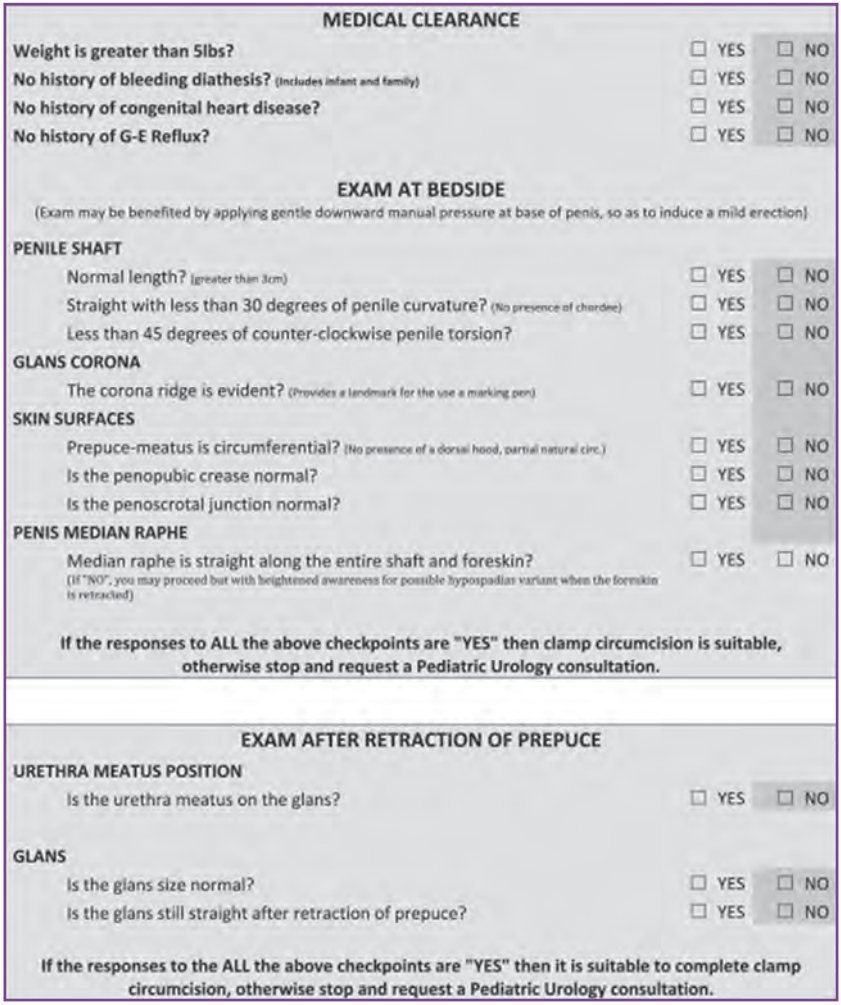


Figure 2-13. The Plastibell circumcision method.

Used with permission from Briggs Medical Service Company.

Surgical circumcision is performed with general anesthesia, typically after 6 months of age. A dorsal penile nerve block, subcutaneous ring block, or caudal anesthetic is routinely used for additional postoperative pain control. The inner and outer foreskin are marked circumferentially, and the skin is removed. Hemostasis is achieved with cautery, and the skin edges are approximated with fine absorbable sutures and/or surgical skin glue.

After newborn circumcision, parents should be instructed to sponge bathe the child until the penis is well healed. After a surgical circumcision, the child is typically able to bathe in 24 to 48 hours. The head of the penis should be fully exposed by pushing back the pubic fat pad, and antibiotic ointment should be applied to the penis with each diaper change for 1 to 2 weeks. It is common for the head of the penis to appear red and swollen for the first 1 to 2 weeks after circumcision. Fibrinous exudate and crusting on the glans are also common and are



MEDICAL CLEARANCE

Weight is greater than 5lbs?	☐ YES	☐ NO
No history of bleeding diathesis? (Includes infant and family)	☐ YES	☐ NO
No history of congenital heart disease?	☐ YES	☐ NO
No history of G-E Reflux?	☐ YES	☐ NO

EXAM AT BEDSIDE

(Exam may be benefited by applying gentle downward manual pressure at base of penis, so as to induce a mild erection)

PENILE SHAFT		
Normal length? (greater than 3cm)	☐ YES	☐ NO
Straight with less than 30 degrees of penile curvature? (No presence of chordee)	☐ YES	☐ NO
Less than 45 degrees of counter-clockwise penile torsion?	☐ YES	☐ NO
GLANS CORONA		
The corona ridge is evident? (Provides a landmark for the use a marking pen)	☐ YES	☐ NO
SKIN SURFACES		
Prepuce-meatus is circumferential? (No presence of a dorsal hood, partial natural circ.)	☐ YES	☐ NO
Is the penopubic crease normal?	☐ YES	☐ NO
Is the penoscrotal junction normal?	☐ YES	☐ NO
PENIS MEDIAN RAPHE		
Median raphe is straight along the entire shaft and foreskin? (If "NO", you may proceed but with heightened awareness for possible hypospadias variant when the foreskin is retracted)	☐ YES	☐ NO

If the responses to ALL the above checkpoints are "YES" then clamp circumcision is suitable, otherwise stop and request a Pediatric Urology consultation.

EXAM AFTER RETRACTION OF PREPUCE

URETHRA MEATUS POSITION		
Is the urethra meatus on the glans?	☐ YES	☐ NO
GLANS		
Is the glans size normal?	☐ YES	☐ NO
Is the glans still straight after retraction of prepuce?	☐ YES	☐ NO

If the responses to the ALL the above checkpoints are "YES" then it is suitable to complete clamp circumcision, otherwise stop and request a Pediatric Urology consultation.

Figure 2-14. Checklist for evaluating the suitability for newborn circumcision.

Reprinted with permission from Concodora CW, Maizels M, Dean GE, et al. Checklist assessment tool to evaluate suitability and success of neonatal clamp circumcision: a prospective study. *J Pediatr Urol*. 2016;12(4):235.e1–235.e5.

often mistaken for pus by parents. If parents are concerned about the appearance of the child's penis after circumcision, the child should be examined by a medical professional. However, most of the time, reassurance about the normal healing process is all that is necessary.

Complications of circumcision include postoperative bleeding and/or hematoma, meatal stenosis, and removal of too much or too little foreskin, as well as rare but clinically significant complications, such as urethral injury or glans amputation. The postoperative complication rate after circumcision on the basis of a multinational review has been estimated at 1.5% (range, 0%–16%), although serious adverse events were rare (median, 0%; range, 0%–2%). Complication rates were higher when the circumcision was performed by a nonmedical provider (eg, ritual circumcisions) and for children aged 12 months to 12 years (complication rate, 6%; range, 2%–14%). Many of the studies included in this review were from resource-poor areas, such as Africa and the Middle East, which tend to report higher complication rates. In contrast, a review of approximately 1.4 million circumcisions in the United States (93.3% performed as newborns) demonstrated a complication rate less than 0.5%. Circumcisions performed after 1 year of age were associated with a 10- to 20-fold higher rate of adverse events when compared with circumcisions performed in infancy.

Care of the Uncircumcised Penis

The foreskin of an uncircumcised boy should never be forcefully retracted by the parents or the patient himself. No special care is needed for boys with physiological phimosis. When the child starts bathing himself, he should be instructed to gently pull back the foreskin and clean underneath the foreskin with soap and water. The foreskin should then be pulled completely back over the head of the penis.

When to Refer

Refer the patient to a pediatric urologist for the following:

- Patient or parental desire for circumcision outside of the neonatal period
- Penile anomalies, including hypospadias, concealed (buried) penis, penoscrotal webbing, chordee, incomplete (dorsal hood) prepuce, and penile torsion (>45°)
- Phimosis refractory to steroid cream
- Lichen sclerosus (BXO)

- Male patients with recurrent balanoposthitis and/or UTIs
- Post-circumcision complications, including symptomatic meatal stenosis, penile bands and skin bridges, penile skin tags and inclusion cysts, and trapped or concealed penis

Clinical Pearls

- Conditions that may be managed by the pediatrician include routine neonatal circumcision, physiological phimosis, preputial adhesions, balanitis, and meatitis.
- *Do not* perform neonatal circumcision in the presence of hypospadias, hooded foreskin, chordee, congenital concealed penis, penoscrotal webbing, or penile torsion (>45°).
- Indications for evaluation in the emergency department include severe phimosis with acute urinary retention, paraphimosis (unable to reduce in the clinic), and post-circumcision bleeding (not controlled with manual compression).

Glossary

Balanitis: Inflammation of the glans penis

Balanitis xerotica obliterans (BXO): See *Lichen sclerosus.*

Balanoposthitis: Inflammation of the glans penis and foreskin

Buried penis: See *Concealed penis; Trapped penis.*

Chordee: Curvature of the penis, most easily discerned with natural or simulated erection

Circumcision: Removal of the foreskin

Concealed penis: A penis that is not externally visible due to concealment or entrapment within the pubic fat; seen with obesity and prominent infant pubic fat or as a complication after circumcision (See also *Trapped penis.*)

Fibrinous exudate: Whitish, crusty, or waxy exudate commonly seen on the glans penis for 1 to 2 weeks after circumcision; often mistaken for pus

Hypospadias: Common congenital penile abnormality in which the urethral meatus is located proximal to the orthotopic meatal location on the ventral aspect of the penis, scrotum, or perineum; often associated with chordee and hooded foreskin

Lichen sclerosus: A fibrosing skin condition primarily found in genital areas; in male patients, this may be associated with phimosis, meatal stenosis, and urethral strictures; this is also referred to as *balanitis xerotica obliterans.*

Meatal stenosis: Narrowing of the urethral meatus, seen in circumcised male patients or in lichen sclerosus

Meatitis: Inflammation of the urethral meatus

Paraphimosis: Entrapment of the foreskin proximal to the glans penis after retraction, usually associated with phimosis or difficult retraction of foreskin; a surgical emergency

Pathologic phimosis: Phimosis associated with scarring of the foreskin or phimosis after puberty

Penile bands: Skin bridges from the penile shaft skin to the glans penis, seen after circumcision; prevent by regular exposure of the penis and application of ointment until the circumcision line is fully healed

Phimosis: Inability to fully retract the foreskin

Physiological phimosis: A natural finding in nearly all newborn boys that consists of attachments of the foreskin to the glans

Posthitis: Inflammation of the foreskin

Preputial adhesions: Adherence of the foreskin to the glans penis without fusion of the skin (see *Penile bands*), which typically resolve without intervention

Secondary phimosis: Inability to retract the foreskin after previous full retractability; may be seen with diabetes or after episodes of balanoposthitis

Smegma: White, cheesy substance found under the foreskin, consisting of sloughed epithelial cells and glandular secretions; aids in separation of adhesions between the foreskin and glans

Squamous cell carcinoma of the penis: A rare cancer in adult men, associated with phimosis, HPV, and poor penile hygiene

Trapped penis: A buried penis due to phimosis and/or scarring after circumcision

Urethrocutaneous fistula: A fistula between the urethra and ventral penile skin, most commonly seen as a complication after hypospadias repair

Resources for Parents

- EBSCO Health. Newborn Circumcision: Yes or No? http://optiongrid.org/option-grids/grid-landing/57 (This is a paid product.)
- American Academy of Pediatrics. Care for an uncircumcised penis. HealthyChildren.org Web site. https://www.healthychildren.org/English/ages-stages/baby/bathing-skin-care/Pages/Care-for-an-Uncircumcised-Penis.aspx. Updated June 19, 2017. Accessed October 16, 2018
- American Academy of Pediatrics. Hypospadias: a birth defect of the penis. HealthyChildren.org Web site. https://www.healthychildren.org/English/health-issues/conditions/genitourinary-tract/Pages/hypospadias-a-birth-defect-of-the-penis.aspx. Updated November 21, 2015. Accessed October 16, 2018

References

1. American Academy of Pediatrics Task Force on Circumcision. Circumcision policy statement. *Pediatrics.* 2012;130(3):585–586
2. American Academy of Pediatrics Task Force on Circumcision. Male circumcision. *Pediatrics*. 2012;130(3):e756–e785
3. Castagnetti M, Leonard M, Guerra L, Esposito C, Cimador M. Benign penile skin anomalies in children: a primer for pediatricians. *World J Pediatr*. 2015;11(4):316–323
4. Concodora CW, Maizels M, Dean GE, et al. Checklist assessment tool to evaluate suitability and success of neonatal clamp circumcision: a prospective study. *J Pediatr Urol*. 2016;12(4):235.e1–235.e5
5. World Health Organization Department of Reproductive Health and Research, Joint United Nations Programme on HIV/AIDS. *Male Circumcision: Global Trends and Determinants of Prevalence, Safety and Acceptability.* Geneva, Switzerland: World Health Organization; 2007. http://apps.who.int/iris/bitstream/10665/43749/1/9789241596169_eng.pdf. Accessed October 16, 2018

6. Moreno G, Corbalán J, Peñaloza B, Pantoja T. Topical corticosteroids for treating phimosis in boys. *Cochrane Database Syst Rev*. 2014;(9):CD008973

7. Palmer LS, Palmer JS. Management of abnormalities of the external genitalia in boys. In: Wein AJ, ed. *Campbell-Walsh Urology.* 11th ed. St Louis, MO: Elsevier Health Sciences; 2015:3368–3398.e9

8. Weiss HA, Larke N, Halperin D, Schenker I. Complications of circumcision in male neonates, infants and children: a systematic review. *BMC Urol*. 2010;10:2

9. El Bcheraoui C, Zhang X, Cooper CS, Rose CE, Kilmarx PH, Chen RT. Rates of adverse events associated with male circumcision in U.S. medical settings, 2001 to 2010. *JAMA Pediatr*. 2014;168(7):625–634

10. Rynja SP, de Jong TP, Bosch JL, de Kort LM. Functional, cosmetic and psychosexual results in adult men who underwent hypospadias correction in childhood. *J Pediatr Urol*. 2011;7(5):504–515

CHAPTER 3

Urogynecology

Jeremy M. West, MD, and Angela M. Arlen, MD

Introduction

Anomalies of female embryogenesis may result in a wide spectrum of problems related to development of the urinary and genital tracts. Clinical abnormalities seen in girls and young women that appear to involve the genitalia alone may be the harbinger of related urinary tract disorders. Abnormalities that manifest in infancy may be easy to recognize secondary to abnormal antenatal ultrasonographic (US) or physical examination findings in the newborn period. Many urogenital malformations, however, are elusive and may become evident only after a clinical problem manifests. The most common urogynecologic disorders that prompt evaluation of the child involve problems of urinary continence and introital abnormalities.

Interlabial Masses

Vaginal masses in infants and young girls are generally referred to as *interlabial masses.* Although many of these lesions arise within the introitus, those arising in the urethra or bladder must be recognized to ensure proper management. Many patients with masses in the vaginal area may have leakage of fluid (ie, urine, pus, transudate). Thorough physical examination of the introitus is mandatory in the complete evaluation of urinary incontinence.

Skene Glands (Paraurethral Glands)

The tubular Skene glands (**Figure 3-1**) arise from the urethral epithelium and are the counterparts to the male prostate gland.

In female patients, these glands may be present at the urethral meatus and hymen. Cysts (tense, yellow, thin walled) partially arising within the urethral meatus but mostly external to it may resemble a bulging hymen associated with hydrometrocolpos, or a prolapsing ureterocele (which is compressible and protruding *through* the urethra). These can be infarcted or filled with pus, in which case they are not compressible. Diagnosis is typically established with physical examination, which demonstrates the classic light-yellow color of the cyst along the urethra and above the vaginal introitus. US may be indicated in cases of concern for urinary tract obstruction and for exclusion of ureterocele. Most cases regress spontaneously, but surgical intervention via incision or resection may be required in rare cases of urethral obstruction.

Figure 3-1. Skene glands in a female newborn.

Bartholin Glands

The major vestibular glands of Bartholin arise from the urogenital sinus and open into the vestibule on either side of the hymen. The main glands lie against the ischiopubic ramus, deep to the bulbospongiosus muscle and cavernous tissue. Blockage of the main ducts of the Bartholin glands may lead to cystic dilation at any age but rarely become infected prior to puberty. Physical examination may demonstrate an enlargement along the lateral side of vaginal introitus (**Figure 3-2**). Management is typically conservative in children.

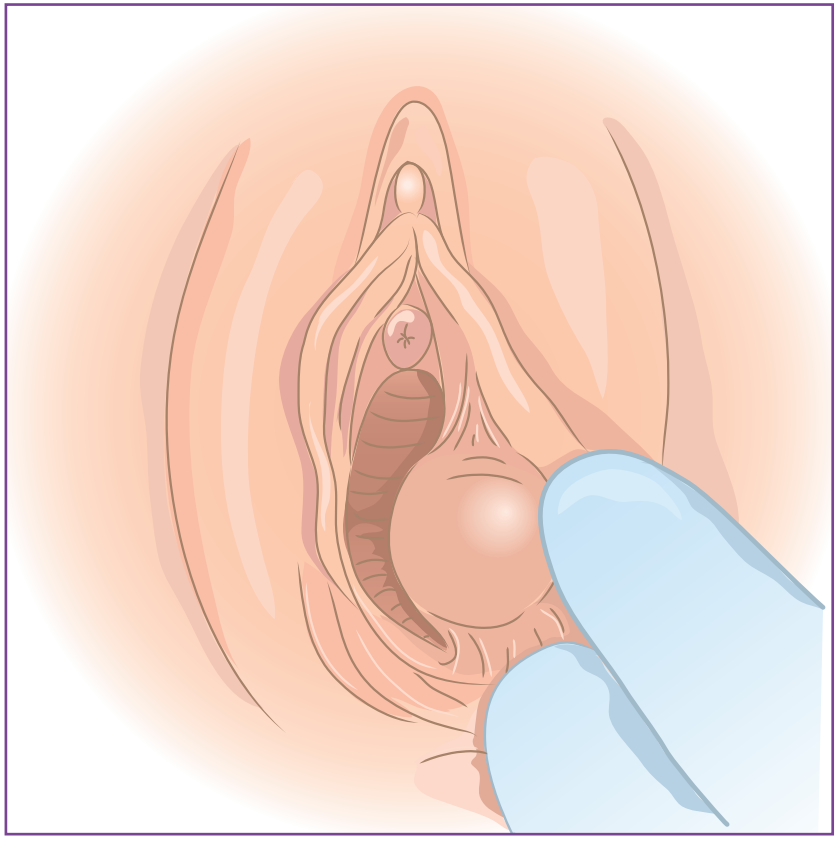


Figure 3-2. Cystic dilation of the Bartholin gland.

Prolapsed Ureterocele

Ureterocele is a dilated distal ureter within the detrusor muscle that may extend beyond the bladder neck (cecoureterocele). Ureteroceles are often associated with an upper-pole renal moiety of a duplicated collecting system and may be ectopic or orthotopic. If a ureterocele extends through the urethral meatus, girls may present with an interlabial or vulvar mass (**Figure 3-3**).

Figure 3-3. External appearance of the prolapsing ectopic ureterocele in a 2-month-old female newborn.

A ureterocele is often detected at US (**Figure 3-4**), but voiding cystourethrography is essential in the evaluation of ureterocele because of the high incidence of concomitant ipsilateral (50%) and contralateral (25%) vesicoureteral reflux. Prompt referral is warranted, and treatment is directed at ureterocele excision, bladder neck reconstruction, and ureteral reimplantation.

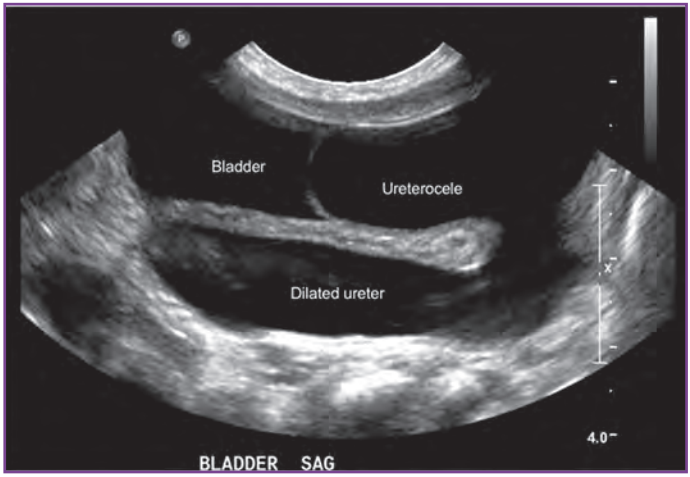


Figure 3-4. Bladder ultrasonographic image of a large, thin-walled ureterocele. Note the hydroureter ipsilateral to the ureterocele.

Hydro(metro)colpos and Imperforate Hymen

Circulating maternal estrogen in the female neonate may result in increased production of cervical mucus. Hydrocolpos and hydrometrocolpos result when mucus collects in the vaginal vault and uterus, respectively. The vaginal orifice may be blocked secondary to an imperforate hymen (**Figure 3-5**), urogenital sinus, or vaginal or uterine atresia. Hydrometrocolpos, by virtue of its abdominal extension, may compress the urethra, rectum, and ureters, resulting in dilation of these structures at US (**Figure 3-6**). Treatment of blockage secondary to a typically located imperforate hymen may involve simple perforation of the hymen when the neonate is in the newborn nursery. If the hymen appears thickened, an incision created with the use of general anesthesia may be required. Higher obstruction involves a more formal approach to treat the associated urogenital abnormalities.

Urethral Prolapse

Eversion of the distal urethral mucosa through the meatus results in a circumferential interlabial lesion (**Figure 3-7**) and is more common in African American girls. Urethral prolapse may be painful, bleed, or weep serosanguinous fluid, prompting medical attention. At examination, urethral prolapse is donut shaped and appears edematous

Figure 3-5. Bulging hymen in a female infant.

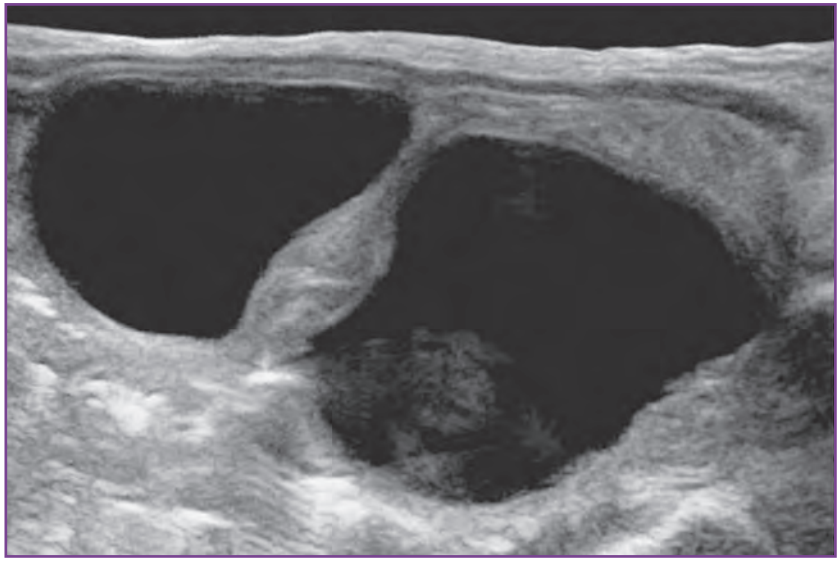


Figure 3-6. Pelvic ultrasonographic image of a female newborn with hydrometrocolpos. Note the bladder positioned anteriorly and the markedly distended vagina positioned posteriorly.

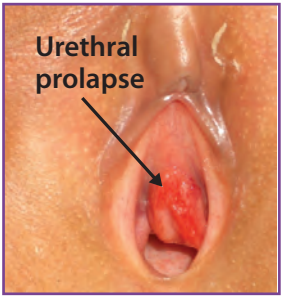


Figure 3-7. Urethral prolapse in a 2-year-old girl who presented with "vaginal" pain and blood spotting.

and congested or even necrotic, with the urethral meatus seen within its center. This lesion should be distinguished from neoplasms of the vagina or bladder. A prolapsed urethra associated with mild edema without necrosis or significant pain may be treated conservatively with sitz baths and estrogen cream over a 2- to 3-week period. Lesions that are causing clinically significant symptoms or urinary retention and those failing to resolve may need to be excised.

Rhabdomyosarcoma

Rhabdomyosarcoma represents the most common soft-tissue sarcoma in infants and children and is the third most common pediatric solid tumor, accounting for 5% to 15% of all pediatric solid tumors (see Chapter 12, Urological Oncology in Pediatrics). Approximately 350 new cases are diagnosed in the United States each year; of these, 15% to 20% arise from the genitourinary tract. Rhabdomyosarcoma of the vagina and bladder (**Figure 3-8**) most commonly appears with vaginal bleeding and a palpable cervical or vaginal mass at presentation.

Classically, a lesion like "a cluster of grapes" (botryoid sarcoma) is visualized as an interlabial mass. Prompt referral for multidisciplinary care is mandatory. Because of the propensity of these lesions to spread, a complete endoscopic and radiographic evaluation is indicated to confirm the diagnosis and rule out local extension and metastatic disease. Primary chemotherapy has resulted in improved bladder salvage and is often curative in the setting of metastatic disease. Surgical excision, with or without radiation therapy, is reserved for post-chemotherapy biopsy-proven residual masses. In recent years, a multimodal approach to genitourinary rhabdomyosarcoma has led to increased survival,

Figure 3-8. Embryonal rhabdomyosarcoma in an 18-month-old girl who initially presented with urinary retention and prolapsed bladder tumor.

as well as pelvic organ preservation. A more thorough discussion of rhabdomyosarcoma may be found in Chapter 12, Urological Oncology in Pediatrics.

Vulvovaginitis

Vulvovaginal issues are the most common gynecologic problem in prepubertal girls. There is an increased propensity for developing vulvovaginitis in this age group because of thinning of the vaginal mucosa and the proximity of the anus to the vagina. These anatomic factors, in combination with a warm, moist environment and an alkaline pH level, make the perineum an ideal location for bacterial growth. Vulvovaginitis is characterized by inflammation, and there is a broad range of symptoms, including itching, pain, discharge, dysuria, odor, vulvar erythema, and even bleeding from epithelial skin breakdown and urinary urgency and frequency (**Figure 3-9**). Approximately 25% to 75% of vulvovaginal presentations in the pediatric population are nonspecific and are often the result of poor hygiene and/or voiding habits, including vaginal voiding, improper wiping, and/or local irritants.

Office evaluation consists of a brief history and external genital examination. Further testing and cultures are rarely indicated. History should include prior episodes, hygiene practices, and any prior treatments

Figure 3-9. Vulvovaginitis in a young girl.

(including over-the-counter lotions and creams). Thorough examination of the external genitalia is mandatory to aid in establishing an accurate diagnosis by evaluating the patient for skin abnormalities, rashes, and signs of sexual abuse.

Infectious Causes

The most common cause of vulvovaginitis is typically secondary to inadequate hygiene. Improper toilet hygiene after voiding or defecation allows pathogens to contaminate and irritate the vagina. Children may also pass respiratory flora from the nose or mouth by direct transmission to the vulvar area manually. Consequently, the most common pathogens are respiratory or enteric in nature, including *Escherichia coli*, *Streptococcus pyogenes, Staphylococcus aureus, Haemophilus influenzae, Enterobius vermicularis,* and, rarely, *Candida albicans* (**Figure 3-10**).

Girls often present with an inflamed, pruritic introitus; perianal redness; and a yellow-green discharge. Vaginal cultures for respiratory and enteric flora should be obtained if the discharge persists or is purulent. Antimicrobial therapy is directed on the basis of the organism isolated. Pinworm (*Enterobius vermicularis*) is the most common helminthic infestation in the United States. If children present with recurrent vulvar and

Figure 3-10. *Candida albicans* vulvovaginitis in an 8-year-old girl with diabetes. Courtesy of Diane Elas; used with permission.

perianal itching predominantly at night, they should be examined and treated empirically.

Infection with *Candida albicans* most commonly manifests as "diaper rash." It is uncommon to develop candidal vaginitis in the pediatric patient because of the alkaline pH level, which prevents the proliferation of fungus. First-line treatment includes good hygiene and application of water-repellent barriers, such as zinc oxide. Girls who are taking antibiotic therapy, or those who are otherwise immunocompromised (ie, diabetes), are more likely to develop candidal vaginitis. Symptoms of vaginal candidiasis include severe vaginal pruritus, soreness, and irritation and sometimes the voiding symptoms of dysuria and frequency. These girls can be treated with a topical or oral antifungal. Nystatin cream should be applied to the affected area twice daily, until complete healing is achieved. Cream is preferred to ointment in intertriginous areas. The most common oral antifungal agent is fluconazole, which can be given as a single 150-mg dose in adolescence for uncomplicated vulvovaginal candidiasis. It is also available in suspension form (a one-time dose of 2 mg/kg).

Lichen Sclerosus

Vulvar lichen sclerosus is uncommon in the pediatric population and is diagnosed by means of visual inspection. Clinical manifestations include itching, vulvar discomfort, discharge, and bleeding. Urinary symptoms, constipation, and behavioral problems are also common in children. Physical examination demonstrates a white, shiny skin plaque, typically in an hourglass configuration around the vagina and anus (**Figures 3-11** and **3-12**). The labia majora and minora are often involved. Biopsy is rarely required in the pediatric population unless atypical or neoplastic changes are suspected. The mainstay for treatment is potent topical steroids, with the goal being alleviation of symptoms and prevention of vaginal introitus narrowing or atrophy of the labia minora. Betamethasone dipropionate 0.05% ointment, diflorasone diacetate 0.05% ointment, or clobetasol propionate 0.05% ointment administered twice daily for 6 to 8 weeks is recommended. There is often, but not always, an associated underlying malignancy in adults. This has not been demonstrated in children; however, long-term follow-up is suggested.

Figure 3-11. Classic lichen sclerosus in a young girl. Erythema is seen with white atrophic patches, and hallmark purpura is observed in a classic "figure 8" pattern.

Reprinted with permission from Dinh H, Purcell SM, Chung C, Zaenglein AL. Pediatric lichen sclerosus: a review of the literature and management recommendations. *J Clin Aesthet Dermatol.* 2016;9(9):49–54.

Figure 3-12. Lichen sclerosus of the vulva and introitus in a 7-year-old girl.
Courtesy of Diane Elas; used with permission.

Labial Adhesions

Labial adhesions are an acquired abnormality of the labial minora; the degree of fusion is variable. Partial fusion is more common posteriorly, with an opening inferior to the clitoral hood (**Figure 3-13**). Labial adhesions occur in an estrogen-depleted environment and are most commonly diagnosed between the ages of 3 months and 3 years. Prepubertal incidence is 0.6% to 3.0%. In most girls, the adhesions are asymptomatic, and no treatment is warranted. Management may be based on the extent of symptoms. The mainstay of therapy is good perineal hygiene. Asymptomatic adhesions should be managed with observation and parental reassurance alone, since up to 80% of cases will resolve spontaneously within a year of diagnosis.

Common symptoms include vulvovaginal irritation, pain with wiping, and postvoid dribbling, since there can be pooling of urine in the vagina behind the adhesions that leaks when the patient stands up. Symptomatic adhesions may be treated with topical conjugated estrogen cream or estradiol ointment, applied with gentle pressure to the adhesion line with a fingertip or cotton swab. Medication is applied twice daily for 2 to 8 weeks, with 50% resolution after 2 to 3 weeks. Refractory symptomatic adhesions, or adhesions causing urinary obstruction, may require mechanical separation. The procedure may be performed in the office with topical lidocaine or general anesthesia, and patients should be referred to an experienced provider. Once separation is achieved, a barrier ointment should be applied for several

Figure 3-13. Partial fusion of the labia minora in a 2-year-old girl.

weeks to prevent recurrence. Recurrence rates are approximately 15% with either manual separation or surgical excision, highlighting the importance of having parents continue to separate the labia after separation by a provider has been completed.

Mayer-Rokitansky-Küster-Hauser Syndrome

Mayer-Rokitansky-Küster-Hauser syndrome is the second most common cause of primary amenorrhea, with an incidence of about 1 in 4,500 to 1 in 5,000 female subjects. This syndrome consists of agenesis of the vagina in genetic female patients (**Figure 3-14**) and may be associated with various other defects of the genitourinary tract.

Most patients present in adolescence with amenorrhea or pain, but Mayer-Rokitansky-Küster-Hauser syndrome may also manifest in young girls with recurrent urinary tract infection or hydrocolpos. Genital defects range from vaginal agenesis alone to agenesis of the uterus and fallopian tubes. These genital anomalies may be associated with (ipsilateral) renal agenesis, so imaging of the upper tracts with US is warranted. Treatment of Mayer-Rokitansky-Küster-Hauser syndrome (vaginal agenesis and solitary kidney) may include progressive vaginal dilation, vaginoplasty, or neovaginal reconstruction with bowel.

Figure 3-14. Vaginal agenesis in a 15-year-old girl with Mayer-Rokitansky-Küster-Hauser syndrome. The arrow indicates urethral meatus.

Female Epispadias

Female epispadias (**Figure 3-15**) occurs in 1 in 480,000 female births and may result in variable presentations, depending on the severity of the urethral defect. In mild cases, the diagnosis may not be apparent until the child remains wet well into childhood. In complete epispadias, incontinence results secondary to *(a)* a foreshortened and widened urethra, *(b)* a partially absent external urethral sphincter, and *(c)* a poorly developed bladder neck. Treatment is directed at reconstruction of these deficient structures and ureteral reimplantation proximal to the reconstructed bladder neck.

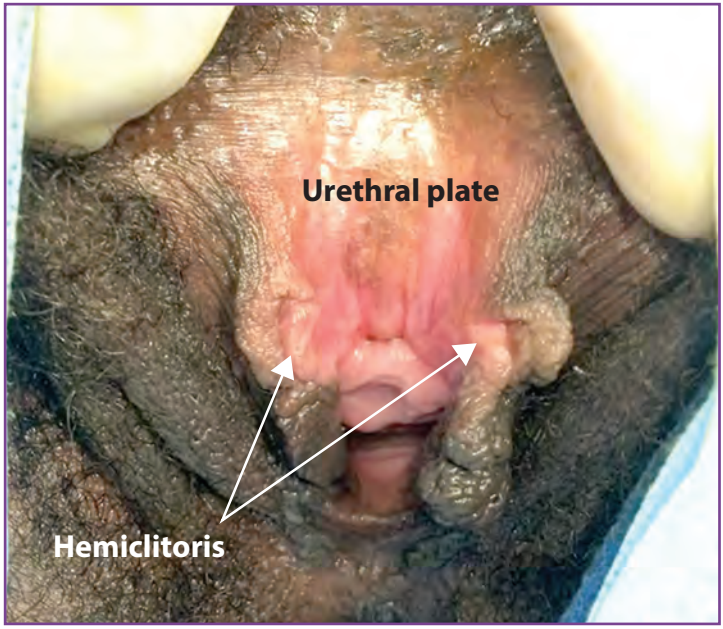


Figure 3-15. Appearance of a postpubertal girl with epispadias who presented with incontinence; note the separation of the labia and clitoris.

Ovarian Masses

Both benign and malignant ovarian tumors are rare in the pediatric population, but the incidence increases with age. Ovarian masses are typically diagnosed because of symptoms such as abdominal pain, distention, or menstrual disorder; physical examination findings; or imaging studies. While malignant ovarian masses in the pediatric population are rare, they are the most common genital neoplasm of childhood. Most ovarian masses are benign, though they can lead to subsequent complications, including torsion, which may appear with severe abdominal and pelvic pain at presentation, with possible loss of the adnexa if diagnosis is delayed. The goal for all ovarian masses in the pediatric population is preservation of sexual and reproductive function. If there is suspicion for an ovarian mass at examination, abdominal US should always be performed (**Figure 3-16**). This can help identify mass characteristics (ie, cystic, solid, complex, or calcified). As with other masses, appropriate referral should be made promptly.

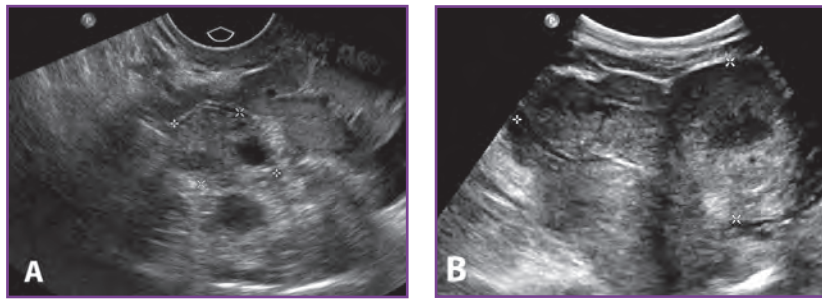


Figure 3-16. Pelvic ultrasonographic images of a female adolescent who presented with right-sided abdominal pain. **A,** A normal-appearing left ovary and a large, lobulated mass in the right pelvis with no normal ovary was identified. **B,** The mass is predominantly solid, with a few small cystic components that are concerning for malignancy.

Ovarian Cysts

Ovarian cysts are common in adolescents but can also occur in the prepubertal child. The overall estimated incidence of ovarian cysts is 1 in 2,500 in the pediatric population. Ovarian cysts are most often referred to as *functional* or *physiological cysts* and consist of follicular, corpus luteum, and theca lutein cysts. In neonates, ovarian cysts are found at antenatal US or as an asymptomatic mass palpated on the abdomen shortly after birth. These are most often related to maternal hormonal stimulation in utero.

In the prepubertal girl, it is less common for physiological cysts to occur as gonadotropin release decreases in early childhood. However, when physiological cysts do occur, they are often associated with precocious puberty. Presenting symptoms typically include abdominal pain, bloating, and possibly vaginal bleeding. US should be performed to rule out ovarian torsion. Further management includes observation with periodic US. If acute rupture with hemorrhage is suspected and is not self-limiting, surgical exploration is warranted. If ovarian cysts are identified on images in combination with onset of early sexual development, referral and evaluation for precocious puberty should be initiated.

Simple or complex ovarian cysts most commonly develop in adolescence. Typical presentation is related to the menstrual cycle of postpubertal girls, with primary symptoms of menstrual irregularities and pelvic pain. The most common type in this age cohort is follicular cysts;

these are a result of the follicle not releasing an oocyte or failing to involute after ovulation. They are typically managed conservatively with serial US examinations (**Figure 3-17**).

If symptomatic or larger than 6 cm, cystectomy can be considered. Some providers may start the child on oral contraceptives to prevent further cysts from developing by suppressing the hypothalamic-pituitary-ovarian axis. If otherwise hemodynamically stable, surgical intervention is deferred, since the cyst will usually resolve with time. If severe symptoms or large cyst size persists, surgical referral is warranted.

Ovarian Teratoma

Ovarian teratomas are a relatively common cause of solid ovarian masses in the pediatric population. Teratomas contain all 3 embryonic germ cell layers and are classified as either mature or immature, which is important when assessing the potential for malignancy. Children may present with the primary symptom of abdominal pain, although some may have a palpable abdominal mass or emesis.

More than one-half of mature teratomas are identified incidentally during surgery or at imaging. Abdominal US of the mature teratoma may demonstrate findings consistent with multiple tissue types, including cartilage, hair, and skin. The presence of calcifications at imaging

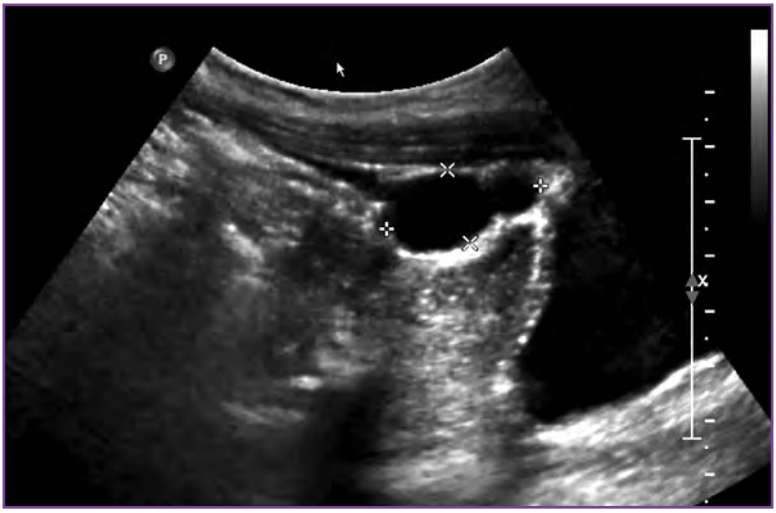


Figure 3-17. A 2-cm left ovarian cyst identified at ultrasonography of the bladder.

is almost diagnostic for mature teratoma. While mature teratomas are benign, there may be the presence of somatic tissue with potential for malignancy, so surgical excision is typically performed. In children, surgical intervention is directed toward preservation of reproductive function via ovary-sparing approaches. Immature teratomas are typically large, solitary, unilateral masses. Unlike mature teratomas, if not treated aggressively, there is a mortality rate of up to 75%. Tumor markers should be obtained, with increased α-fetoprotein and β-human chorionic gonadotropin levels in most cases. Open surgical excision is standard of care, with any suspicious implants also resected. Surgery is generally curative, without the need for chemotherapy in low-grade teratomas. In higher-grade teratomas, surgery plus adjuvant chemotherapy is recommended.

Ovarian Malignancy

Ten percent of pediatric ovarian masses are malignant, with an incidence of 0.5 to 0.7 in 100,000 female subjects aged 0 to 18 years. Presenting symptoms include abdominal pain, increase in abdominal girth, and unexplained nausea or vomiting. The most common tumors in adolescents are germ cell tumors. Initial evaluation is conducted with US to assess the overall size, associated free fluid, and pattern of blood supply. Magnetic resonance imaging or computed tomography can be performed to help further characterize the mass. Baseline tumor markers should be obtained, including α-fetoprotein, lactate dehydrogenase, human chorionic gonadotropin, carcinoembryonic antigen, and cancer antigen 125. For all malignancies, prompt referral to oncology, gynecology, and surgery is warranted.

Resources for Parents

- Center for Young Women's Health. Labial adhesions: a guide for parents. http://youngwomenshealth.org/parents/labial-adhesions-parent. Updated June 14, 2016. Accessed October 16, 2018
- SickKids hospital staff. Vulvovaginitis. AboutKidsHealth Web site. https://www.aboutkidshealth.ca/vulvovaginitis. Updated November 10, 2009. Accessed October 16, 2018

Clinical Pearls

- Girls who present with urinary incontinence or voiding symptoms should undergo a thorough examination of the external genitalia.
- Urethral prolapse appears edematous, with the urethral meatus seen within its center, and should be differentiated from bladder or vaginal malignancy.
- Nonspecific vulvovaginitis is common in the pediatric population and can often be treated successfully with proper hygiene and bladder regimen.
- Asymptomatic labial adhesions should be managed with good perineal hygiene, observation, and parental reassurance alone.
- Ovarian tumors in children are heterogeneous and require prompt referral.

Suggested Readings

Stephens FD, Smith ED, Hutson JM. *Congenital Abnormalities of the Urinary and Genital Tracts*. Oxford, United Kingdom: Isis Medical Media; 1996

Arlen AM, Snyder HM, Kirsch AJ. Pediatric urogynecology. In: Cardozo L, Staskin D, eds. *Textbook of Female Urology and Urogynecology.* 4th ed. Boco Raton, FL: Taylor & Francis; 2016:1256–1270

Hoefgen HR, Merritt DF. Vulvovaginitis. In: Kliegman RM, ed. *Nelson Textbook of Pediatrics.* 20th ed. Philadelphia, PA: Elsevier; 2016:2607–2613

Vilano SE, Robbins CL. Common prepubertal vulvar conditions. *Curr Opin Obstet Gynecol.* 2016;28(5):359–365

CHAPTER 4

Cryptorchidism

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Introduction

Cryptorchidism, or undescended testis, is the absence of one or both testes from the dependent scrotum and is the most common disorder of the male endocrine glands in children. Treatment of the cryptorchid testis is warranted mainly because of the increased risk of infertility and malignancy in the undescended testis. Additionally, these testes may be at increased risk for testicular torsion and, later, there may be psychological effects from having an empty scrotum. The current standard of care in the United States is to perform an orchiopexy, which is surgical correction to reposition the testis into the scrotum. Earlier correction, especially in boys younger than 18 months, is particularly important to decrease the risks of infertility and cancer. After orchiopexy, boys can receive annual genital examinations like any other boy from the primary care provider, as well as guidance on performing self-testicular examinations starting at puberty. In 2014, the American Urological Association (AUA) released a guideline on the evaluation and treatment of cryptorchidism, and throughout this chapter, statements from this guideline will be referenced.

Incidence

Cryptorchidism is the most common congenital genitourinary condition in male infants and is diagnosed in 3% of full-term boys. Spontaneous testicular descent may occur within the first 3 months, and by 6 months after birth, only 1% of boys still have undescended testes. There are believed to be 2 peaks for diagnosis of

cryptorchidism—at birth and between 5 and 7 years of age. While most cases are diagnosed at birth, the increased detection rate at 5 to 7 years is thought to be secondary to linear body growth, which causes a low undescended testis to become difficult to palpate or reside in a higher location ("ascending testis"). Incidence of cryptorchidism increases inversely with gestational age at birth, and as newborns, preterm boys have rates as high as 15% to 45%. Bilateral undescended testes occur in 10% of boys with cryptorchidism. In 5% of boys, unilateral anorchia (absence of the testis) is ultimately determined as the etiologic origin of the nonpalpable gonad.

Embryology and Testicular Descent

Testicular descent is a complex process, and its specific details and critical hormones and factors are poorly understood. Despite this, what is known about the development of the testes and testicular descent from human and animal studies is important in understanding the possible etiology for and locations of the undescended testis. The undifferentiated gonad in the developing embryo begins to form adjacent to the mesonephros (second rudimentary kidney) in the abdomen, and by 6 to 8 weeks of gestation, the gonad forms testicular cells under the influence of the *SRY* gene on the Y chromosome. Some of these cells include Leydig cells, which begin to secrete hormones (especially insulinlike growth factor 3 and androgens) thought to be important in bringing the testicle down to the internal inguinal ring (by approximately 22–25 weeks of gestation). At the same time this transabdominal phase of descent is occurring, the processus vaginalis (an invagination of the peritoneum that begins at the internal inguinal ring and proceeds through the inguinal canal and into the scrotum) forms, and the gubernaculum (a caudal inguinoscrotal ligament that connects the testis to the internal inguinal ring and, eventually, with the scrotum) begins to develop. Finally, under the influence of androgens and likely neuromuscular effects, the testis undergoes transinguinal descent and assumes its position in the scrotum by the beginning of the third trimester (in the seventh month of gestation) in most fetuses (**Figure 4-1**). The course of normal descent explains the possible locations of the cryptorchid testis, from high up in the abdomen adjacent to the kidney to just proximal to the internal inguinal ring or low in the inguinal canal.

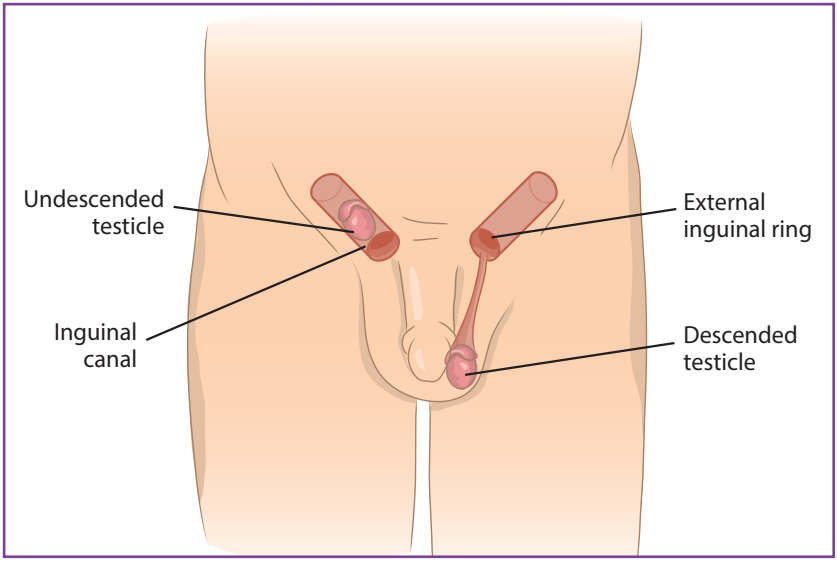

Figure 4-1. How the testicles descend into the scrotum in utero.

Two other important observations come from an understanding of the embryology of testicular development and descent. First, the fact that descent is not complete until the third trimester in most boys explains the higher incidence of cryptorchidism seen in preterm boys. Second, the influence of androgens and hormones on testicular descent, especially in the transinguinal phase, is one possible explanation for the increased rate of spontaneous testicular descent in the first 3 months after birth. Around 60 to 90 days after birth, the neonate normally undergoes what is often referred to as a "mini-puberty," when there is a surge of gonadotropins (including luteinizing hormone [LH] and follicle-stimulating hormone [FSH]). This surge of LH, FSH, and testosterone may result in spontaneous testicular descent at this time, especially in preterm boys.

Pathophysiology

The cryptorchid testis shows evidence of abnormal development and maturation as early as 3 months postnatally. In the normal testis, fetal gonocytes differentiate into adult dark spermatogonia at 4 to 5 months of age, and these adult dark spermatogonia become primary spermatocytes at 5 years after birth. These steps may be abnormal in the

cryptorchid testis, and in addition, the thermal effects of the incorrectly located testis on spermatogenesis and maturation are compounded after 18 months of age. In both human and animal studies, the germ cell abnormalities seen in the undescended testis can also be seen, to a lesser extent, in the contralateral descended testis. Some studies have suggested a blunting of the LH-FSH surge ("mini-puberty") in boys with cryptorchidism who continue to have undescended testis 1 year after birth when compared with those with postnatal spontaneous testicular descent. Additionally, boys with cryptorchidism have lower morning urinary LH levels and a decreased gonadotropin response to gonadotropin-releasing hormone. These hormonal differences and lack of the LH-FSH surge are thought to play a role in failure of germ cell maturation and possible future subfertility in boys with cryptorchidism. Subsequent studies, however, have shown inconsistent results with regard to testosterone, LH, and FSH levels in boys with cryptorchidism when compared to control subjects; thus, the influence of hypogonadotropic hypogonadism in the pathophysiology of cryptorchidism is still unclear.

Etiologic Origins

In most cases of isolated cryptorchidism, the specific etiologic origin is unknown, and studies indicate a multifactorial disease process that involves numerous genetic and environmental risk factors. Familial studies of boys with cryptorchidism show the anomaly in 23% of family members of patients, compared with only 7.5% of family members of control subjects. Furthermore, 4% of fathers of cryptorchid boys, 6% to 10% of brothers of cryptorchid boys, and 27% of monozygotic twins of cryptorchid boys also have a history of undescended testes. Data suggest that the disease is polygenic, involving multiple genes, with a complex interaction pattern rather than 1 or 2 dominant genetic loci. In addition to a family history of cryptorchidism, several studies have demonstrated additional perinatal risk factors, including preterm birth, low birth weight, breech presentation, small size for gestational age, advanced maternal age, and maternal diabetes.

To date, cryptorchidism has been found to be a component of more than 500 medical syndromes and approximately 200 genes have been linked to undescended testis. Most cases, however, are isolated anomalies with a ratio of 6:1 for nonsyndromic to syndromic cryptorchidism in 1 large study. Some syndromes that are associated with

cryptorchidism include prune belly, Klinefelter, Down, Noonan, Prader-Willi, complete androgen insensitivity, and 22q11.2 microdeletion syndromes.

Given that most cryptorchidism cases are spontaneous and isolated, the role of environmental risk factors, especially those in the maternal environment during fetal development, have been examined. Epidemiology and population-based studies have indicated numerous possible environmental factors, including endocrine-disrupting chemicals (EDCs), maternal alcohol consumption, maternal smoking, and maternal analgesic use. Concerns over EDCs began after a report on the higher risk of cryptorchidism related to maternal exposure to diethylstilbestrol. Other EDCs studied (pesticides, flame retardants, and phthalates) have been postulated to cause cryptorchidism as part of a "testicular dysgenesis syndrome" that also includes hypospadias and infertility. The epidemiological findings, however, do not support environmental EDCs as a strong cause of increased susceptibility to cryptorchidism in humans.

Outcome and Prognosis

The 2 major concerns with cryptorchid testes are future infertility and malignancy risk. It is uncertain whether surgery will completely reverse the maturational failure and spermatogenesis abnormalities of the undescended testis, but relocation of the testis to the scrotum can prevent continued thermal injury and allows easy palpation of the testis to monitor for masses or lesions.

Fertility

Despite the fact that as many as 18% to 43% of men with unilateral cryptorchidism will have abnormal semen quality or reduced sperm counts, paternity is achieved in less than or equal to 90%, which is similar to paternity rates of unaffected men in the general population. Bilateral cryptorchidism, however, is associated with abnormal semen quality in up to 75% to 100% of affected men and with a reduced rate of paternity, as low as 65% in one study. Earlier orchiopexy in boys younger than 1 to 2 years has been associated with greater catch-up growth (ability of originally smaller cryptorchid testis to grow to size of contralateral unaffected testis), improved total sperm counts, and sperm motility. Testicular histologic studies also show greater seminiferous tubular diameter and higher germ cell and Leydig cell counts in

male infants who undergo orchiopexy at younger than 1 year than in boys who undergo surgery at older than 1 year. Given these findings, the AUA guideline on cryptorchidism recommends as a standard (based on grade B evidence [research evidence]) that surgical correction be performed between 6 and 18 months (corrected for gestational age) in all boys who do not have spontaneous testicular descent by 6 months.

Testicular Malignancy

Several studies have shown an association between increasing age at orchiopexy and risk of testicular cancer. According to recent studies, the relative risk of cancer in the undescended testis has been estimated to be between 2.5 and 8.0. Historically, intra-abdominal testes were believed to be at higher risk for malignancy than testes located in the inguinal canal, but because of the likely inclusion of syndromic cryptorchidism in these earlier studies, this difference is unclear. Regardless of location, numerous studies have shown a 2- to 6-times reduction in the relative risk of cancer in favor of prepubertal orchiopexy when compared with postpuberty orchiopexy. One systematic review and meta-analysis yielded an odds ratio of 3.4 for testicular cancer risk in boys who never underwent surgery or had orchiopexy performed after the age of 10 years, when compared with boys who underwent orchiopexy before the age of 10 years. These findings, in addition to the fertility concerns discussed earlier, strongly support the AUA guideline statement for orchiopexy between 6 and 18 months after birth.

Interestingly, the contralateral descended testis has also been shown to have an increased risk of malignancy in some studies, accounting for as many as 15% of tumors in these boys. The risk in these studies is lower than that in the affected ipsilateral undescended testis. Other studies, however, show no increased risk of cancer in the contralateral testis; thus, future well-designed prospective studies with long-term follow-up are needed to better answer this clinical question.

The AUA guideline on cryptorchidism recommends as a clinical principle that providers counsel boys with a history of cryptorchidism and their parents about the potential long-term risks of infertility and cancer. All boys with previous cryptorchidism should be taught at the beginning of puberty how to perform monthly testicular self-examination as a method for possibly detecting cancer at an early stage. These recommendations are the same for any boy at puberty, but

educating of the patient with cryptorchidism about his increased risk of cancer and the high success rates of testicular cancer treatment, especially when the cancer is diagnosed early, is of critical importance.

Diagnosis

History

While the diagnosis of cryptorchidism is based on physical examination findings, appropriate patient history compilation can offer clues as to the etiologic origin and likelihood of spontaneous descent. The history should focus on the known risk factors for cryptorchidism, including preterm birth (specifically, gestational age in weeks at the time of birth and current corrected age), birth weight, maternal diabetes, exogenous maternal hormone use (ie, infertility treatment), previous inguinal surgery, central nervous system lesions (ie, myelomeningocele or cerebral palsy), precocious puberty, and other congenital anomalies.

In addition, one should note whether the testes were palpable in the scrotum at the time of birth or at any time in the first 6 months after birth. Experts describe 2 types of cryptorchidism: *(a)* congenital, in which the undescended testis is present at birth or first noted within the first 6 months after birth, and *(b)* acquired, in which the testes are noted to be in the scrotum at birth but are no longer palpable in the scrotum at a later time. "Acquired" cryptorchidism is likely a primary failure of complete testicular descent, and the testis may first manifest as undescended during somatic growth, when the distance between the inguinal canal and scrotum lengthens, particularly around 7 to 10 years of age. These testes are associated with similar histopathologic changes observed in cryptorchid testes noticed at birth, and these boys should be referred to an appropriate surgical specialist at the time of diagnosis.

Physical Examination

The diagnosis of the undescended testis is based on physical examination findings, and the cryptorchid testis may be located in the abdomen, the inguinal canal, the superficial inguinal pouch (just outside of the external inguinal ring), or the upper scrotum, or it may be in an ectopic location (toward the perineum, contralateral scrotum, medial thigh, or femoral region). Testicular position may change at each subsequent

visit (in either a proximal or distal direction); thus, primary care providers should palpate the testes for quality and position at each health supervision visit. A genital examination is warranted at each visit prior to puberty, regardless of prior documentation of descended testes, even after the first few years after birth, because of the possibility of "acquired" cryptorchidism or an "ascending" testis after previous inguinal surgery.

A proper genital examination in boys begins with an observation of the scrotum, with the infant or child supine, in the frog-leg position. Underdevelopment of one hemiscrotum can be the first indication that a testis is undescended, and properly descended testes can often be visually identified in their ipsilateral hemiscrotum without palpation. If the testis is not readily palpable, a thorough examination should begin with a sweep with one warmed hand from the anterior superior iliac spine medially over the inguinal canal, toward the ipsilateral hemiscrotum. Some clinicians favor standing on the same side as the cryptorchid testis, while others prefer sweeping with their nondominant hand. The best patient and hand positioning for the examination is dependent on the experience of the individual examiner and must be that which is most comfortable. If the testis is palpated, an attempt should be made to use the non-sweeping hand to grasp the testis from below and to bring it toward the scrotum while the sweeping hand continues to apply superior pressure and additional sweeps as necessary. Sometimes the testis can be brought into its ipsilateral hemiscrotum but appears to be tethered or under tension. By maintaining the testis in the scrotum for a minute, the cremasteric reflex can be fatigued. At this point, the testis should be released, and if it remains in the scrotum, it is likely a retractile testis and not truly cryptorchid. On the other hand, if the testis immediately recoils back out of the scrotum, it is a true undescended testis. If the testis is not easily palpable, applying a lubricating jelly or soap (ie, liquid soap, not an alcohol-based instant sanitizer) over the inguinal region and then re-sweeping may assist in identifying the testis or detecting the subtle impression of the pulled testis retracting proximally back toward the internal inguinal ring. Appropriate documentation of physical examination findings at each visit, including location of the undescended testis, as well as size and consistency of the testis— especially in comparison to the contralateral testis—is critically important.

Retractile testes are those that appear to be undescended but are, in fact, descended with a brisk cremasteric reflex. When the medial part of the thigh is touched, the cremasteric muscle contracts, which can cause the testis to pull up toward the inguinal canal (**Figure 4-2**). This cremasteric reflex is often more prominent and brisk in infants and young boys and diminishes with age. While retractile testes have normal fertility and malignancy potential, some feel that these testes are at a higher risk of ascending, resulting in "acquired" cryptorchidism.

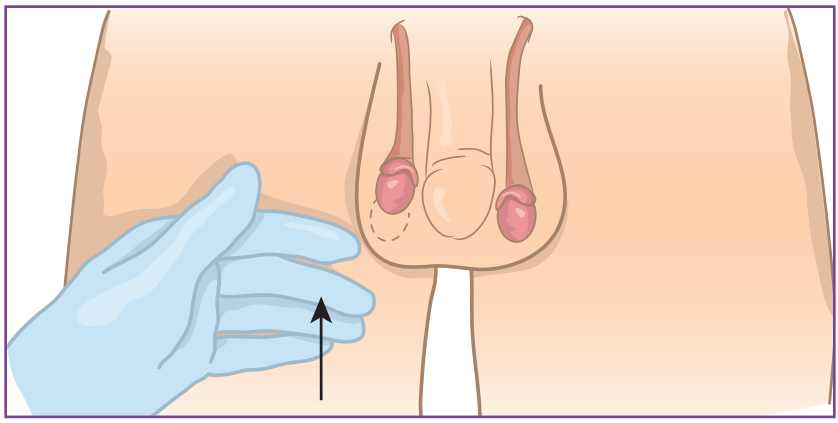

Figure 4-2. Illustration of the cremasteric reflux. When the medial part of the thigh is touched, the cremasteric muscle contracts, which can cause the testis to pull up toward the inguinal canal.

Evaluation

For the typical boy with unilateral palpable or unilateral nonpalpable cryptorchid testis, no additional workup, either laboratory evaluation or imaging studies, is necessary. Boys with cryptorchidism at birth should be referred to a pediatric urologist if spontaneous descent has not occurred by 6 months of age. Furthermore, all boys with the possibility of newly diagnosed or acquired cryptorchidism after 6 months of age should also be referred to a surgical specialist.

Imaging studies (ultrasonography [US], computed tomography [CT], or magnetic resonance [MR] imaging) can be used to detect cryptorchid testes, but these studies are only accurate for those located in the inguinal region, where they are also usually easily palpable. The

accuracy of imaging studies for the detection of intra-abdominal testes is less than 50%, and since the standard of care for these nonpalpable testes is examination with anesthesia, open inguinal exploration, or diagnostic laparoscopy, there is minimal gain from performing these studies preoperatively. In other words, when the imaging study indicates an undescended testis, the testis is likely palpable at examination, and when the imaging study is unable to show an undescended testis, the diagnostic accuracy is too low to forego the need for surgical exploration. Therefore, there is no role for preoperative imaging studies in boys with cryptorchidism, and the AUA guideline specifically recommends as a standard that providers "should not perform US or other imaging modalities" in the evaluation of boys with cryptorchidism, as these studies "rarely assist in decision making" (according to grade B evidence [research evidence]).

For the patient with bilateral cryptorchidism in which one testis is palpable, no further workup is necessary, as long as there are no other concerning findings in the history or at physical examination (**Figure 4-3**).

The patient with bilateral nonpalpable testes, however, requires consultation with an appropriate specialist (pediatric endocrinologist, geneticist, and urologist) and workup that includes a chromosomal and endocrinologic evaluation (AUA standard statement, grade B evidence [research evidence]). The concern in these patients is the possibility of a disorder of sex development (DSD), and all phenotypic male newborns with bilateral nonpalpable testes require immediate workup with karyotype and hormonal serum laboratory studies, including 17-hydroxyprogesterone, LH, FSH, testosterone, and androstenedione, to rule out congenital adrenal hyperplasia (CAH). DSD should also be assessed in newborns with unilateral or bilateral cryptorchidism and phallic anomalies (ie, hypospadias or microphallus). In boys with bilateral nonpalpable testes in whom CAH and other DSD conditions have been ruled out, providers should consider obtaining antimüllerian hormone and/or inhibin serum levels as a test to confirm the presence of testicular tissue. Anorchid boys (ie, boys with absences of both testes) will have undetectable levels of both hormones and will also have high levels of LH-FSH and fail to respond to human chorionic gonadotropin stimulation with increased testosterone levels. Laparoscopy can also be used to confirm the presence or absence of bilaterally nonpalpable testes.

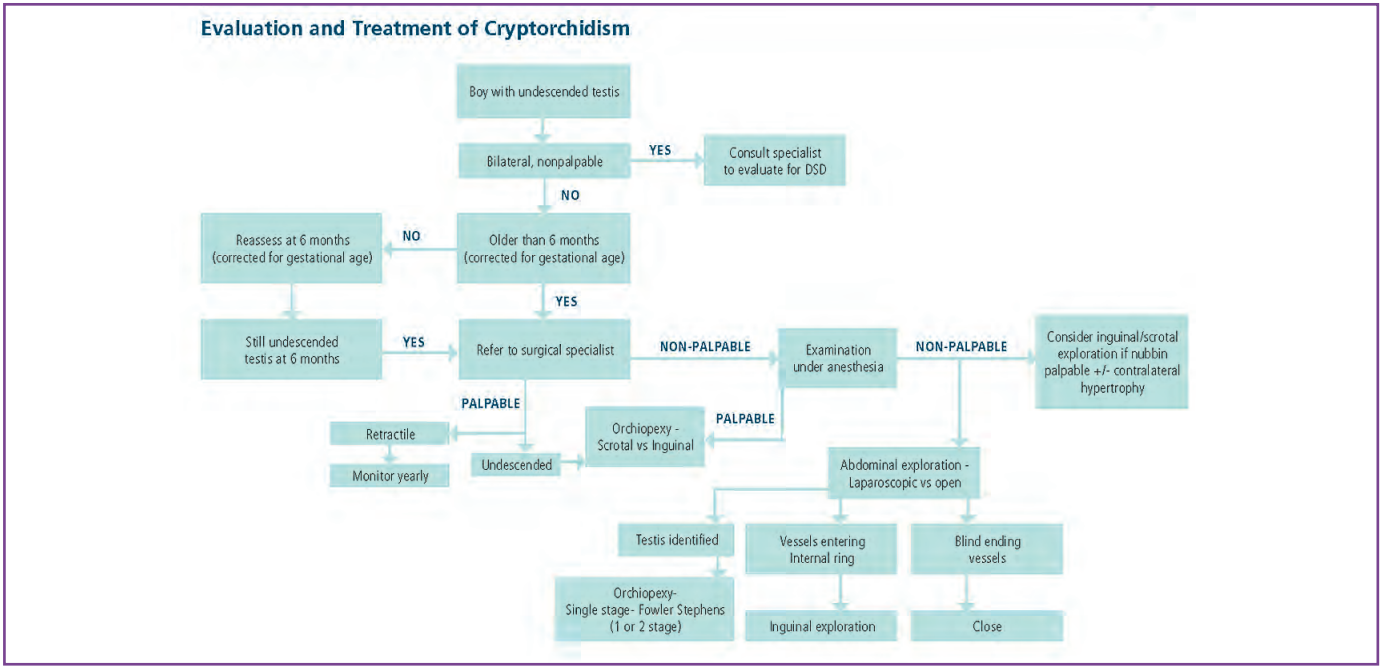

Figure 4-3. Algorithm for evaluation and treatment of cryptorchidism as proposed in the American Urological Association guideline on cryptorchidism.

Reprinted with permission from Kolon TF, Herndon CD, Baker LA, et al; American Urological Association. Evaluation and treatment of cryptorchidism: AUA guideline. *J Urol.* 2014;192(2):337–345. http://www.auanet.org/documents/education/clinical-guidance/Cryptorchidism-Algorithm.pdf. Accessed October 16, 2018. Copyright ©2014, American Urological Association Education and Research, Inc.

Differential Diagnosis

The differential diagnosis for cryptorchidism includes retractile testes, atrophic or "vanishing" testes, and DSD. Retractile testes are commonly mischaracterized as undescended testes. True retractile testes can be distinguished from undescended testes on the basis of physical examination, in which the testes remain in the scrotum for some time after the cremasteric muscle is overstretched and fatigued. Atrophic or "vanishing" testes are thought to be lost secondary to neonatal vascular ischemia or an in utero event, such as torsion. Boys with unilateral atrophic testis often have contralateral testicular hypertrophy, although this is not a reliable diagnostic sign to confirm the absence of the contralateral testicle. As mentioned, all infants and children with bilateral nonpalpable testes should undergo a chromosomal and endocrine evaluation, with referral to the appropriate pediatric specialists. Up to 30% to 40% of patients with cryptorchidism and concomitant hypospadias are found to have a DSD.

Treatment Options and Outcomes

Hormone Therapy

Use of gonadotropin-releasing hormone and human chorionic gonadotropin to induce descent of the cryptorchid testis has been widely used in Europe. Acute success rates with both forms of hormonal therapy range between 30% and 50%, but less than 20% remain descended with long-term follow-up. Hormonal therapy for this indication is not approved in the United States; thus, this treatment is rarely used. Furthermore, the AUA guideline on cryptorchidism includes a standard statement against the use of hormonal therapy to induce testicular descent.

Surgery

The goals of surgically bringing the testis into the scrotum (ie, orchiopexy) are to prevent future thermal damage to the testis, fix an associated inguinal hernia sac (seen in almost all cases of congenital cryptorchidism), prevent testicular torsion or injury against the pubic bone, avoid the psychological effects of an empty scrotum, and allow for easy future palpation (ie, for testicular self-examinations at puberty).

Orchiopexy can be achieved by scrotal, inguinal, abdominal incision or laparoscopy. Orchiopexy is most commonly achieved via an inguinal incision, especially in infants, since this approach allows simultaneous hernia correction. Scrotal incision is usually reserved for the older boy with "acquired" cryptorchidism, when the testis can easily be brought into the scrotum and in whom the risk of concomitant hernia is lower. Exploration for the nonpalpable testis is often performed via laparoscopy or an inguinal incision. In certain cases of high intra-abdominal testes, the internal spermatic artery may be tethering the testis and preventing it from being brought down to the ipsilateral hemiscrotum (**Figure 4-4**).

When this occurs, the artery may be ligated, and the testis is left to survive on the blood supply from the vas deferens and the cremasteric arteries, which are longer (**Figure 4-5**).

This procedure is known as *Fowler-Stephens orchiopexy* and may occur in 1 stage (ie, the testis is brought down to the scrotum at the same time that the spermatic artery is divided) or 2 stages (ie, the testis is left in its intra-abdominal location after artery division and only brought down later, during a second surgery).

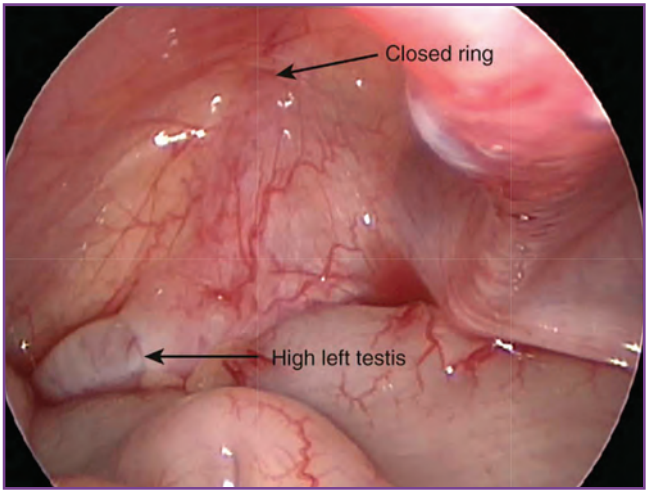

Figure 4-4. High intra-abdominal testis identified at laparoscopic evaluation. A left testis identified high in the abdomen is associated with a closed internal ring.

Reprinted with permission from Barthold JS, Hagerty JA. Etiology, diagnosis, and management of the undescended testis. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 11th ed. Philadelphia, PA: Elsevier; 2016:3430–3452.

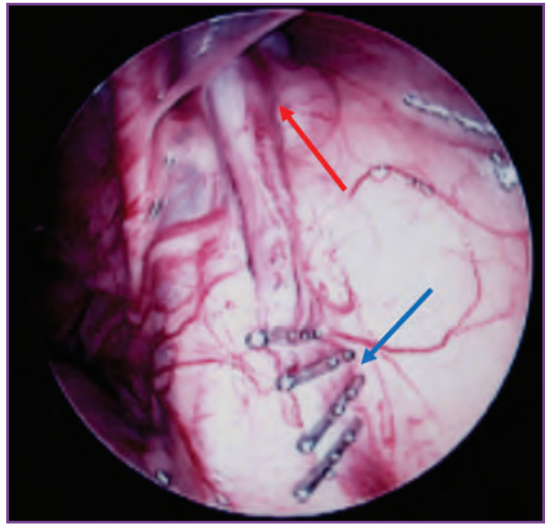

Figure 4-5. Intraoperative laparoscopic image of the ligation of the spermatic vessels with laparoscopic clips (blue arrow) as part of the first stage of the Fowler-Stephens orchiopexy used for an intra-abdominal testicle (red arrow) that is tethered by short spermatic vessels.

When the contralateral testis is normal, orchiectomy (ie, surgical removal of the testis) for the intra-abdominal testis may be necessary in extremely difficult cases, such as when the identified testis is dysmorphic or severely hypoplastic or when either the spermatic vessels or vas deferens is very short. Additionally, orchiectomy in the setting of a normal contralateral testis should be considered in any boy or man who presents after puberty, given the risk of malignancy.

Follow-up

Routinely, the first examination occurs by 6 weeks and again 6 to 12 months later, to check on testicular size and position. Furthermore, all boys should be examined by the primary care provider with full genital examinations at each health supervision visit. During puberty, patients should be seen again to confirm proper location of the testes and explain the technique for monthly testicular self-examination for early testis cancer detection.

When to Refer

- Patients with cryptorchidism should be referred to a pediatric surgical specialist when there is no spontaneous testicular descent by 6 months of age (corrected for gestational age).
- Patients with a new diagnosis of cryptorchidism after 6 months of age (corrected for gestational age) should be referred to a pediatric surgical specialist.
- Immediate consultation with a pediatric specialist should be undertaken for all phenotypic male newborns with bilateral, nonpalpable testes for evaluation of possible DSD.
- Consult a pediatric specialist for all patients with cryptorchidism (unilateral or bilateral) and phallic anomalies (ie, hypospadias or microphallus).

Clinical Pearls

- Perform a thorough genital examination—including scrotal examination—at every health supervision visit for palpable testes, regardless of age and prior examination findings.
- Imaging studies (eg, US, CT, MR imaging) should not be performed or ordered by the primary care provider in the evaluation of cryptorchidism prior to referral to a pediatric urologist.
- Refer *(a)* any patient with cryptorchidism at 6 months of age and *(b)* those with newly diagnosed cryptorchidism to a pediatric urologist.
- The ideal timing for surgery for cryptorchidism is between 6 and 18 months of age and should occur before puberty to reduce the risk of malignancy and minimize infertility.
- While spermatogenic function is reduced to some extent, in most male patients with a history of cryptorchidism, unilateral undescended testes yield similar paternity rates as those of unaffected male subjects in the general population.
- The long-term risk of testicular malignancy exists, even after successful surgical correction, although evidence suggests that earlier orchiopexy may reduce this risk.

Resources for Parents

- American Academy of Pediatrics. Undescended testicles. HealthyChildren.org Web site. https://www.healthychildren.org/English/health-issues/conditions/genitourinary-tract/Pages/Undescended-Testicles.aspx. Updated November 21, 2015. Accessed October 16, 2018
- Urology Care Foundation. What are undescended testicles (cryptorchidism)? http://www.urologyhealth.org/urologic-conditions/cryptorchidism. Accessed October 16, 2018
- KidsHealth. Undescended testicles. http://kidshealth.org/en/parents/cryptorchidism.html. Reviewed February 2017. Accessed October 16, 2018

Suggested Readings

Barthold JS, Hagerty JA. Etiology, diagnosis, and management of the undescended testis. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 11th ed. Philadelphia, PA: Elsevier; 2016:3430–3452

Docimo SG. The results of surgical therapy for cryptorchidism: a literature review and analysis. *J Urol*. 1995;154(3):1148–1152

Kolon TF, Herndon CD, Baker LA, et al; American Urological Assocation. Evaluation and treatment of cryptorchidism: AUA guideline. *J Urol*. 2014;192(2):337–345. http://www.auanet.org/documents/education/clinical-guidance/Cryptorchidism-Algorithm.pdf. Accessed October 16, 2018

Pettersson A, Richiardi L, Nordenskjold A, Kaijser M, Akre O. Age at surgery for undescended testis and risk of testicular cancer. *N Engl J Med*. 2007;356(18):1835–1841

Ritzén EM. Undescended testes: a consensus on management. *Eur J Endocrinol*. 2008;159(Suppl 1):S87–S90

Virtanen HE, Bjerknes R, Cortes D, et al. Cryptorchidism: classification, prevalence and long-term consequences. *Acta Paediatr*. 2007;96(5):611–616

Wayne C, Chan E, Nasr A; Canadian Association of Paediatric Surgeons Evidence-Based Resource. What is the ideal surgical approach for intra-abdominal testes? A systematic review. *Pediatr Surg Int*. 2015;31(4):327–338

Wood HM, Elder JS. Cryptorchidism and testicular cancer: separating fact from fiction. *J Urol*. 2009;181(2):452–461

CHAPTER 5

Inguinal and Scrotal Problems

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Hernia

Introduction

Inguinal hernia is one of the most common surgical conditions in infants and children. Inguinal hernias are protrusions of a portion of an abdominal organ or tissue into the groin, which can be categorized into *indirect* and *direct* hernias. Almost all inguinal hernias (>95%) in neonates, infants, and children are indirect hernias that protrude through a persistently patent processus vaginalis that provides an open communication between the abdominal cavity and inguinal canal or scrotum through the internal inguinal ring. Direct hernias are protrusions of abdominal contents through a weak point in the abdominal wall fascia that occur medial to the inferior epigastric vessels and are the most common types of hernias seen in adults. The focus of this section will be on indirect inguinal hernias encountered in the child and adolescent population.

Pathophysiology and Embryology

The processus vaginalis is an embryological connection between the abdominal cavity and the scrotum that begins at the internal inguinal ring and traverses the inguinal canal. It is a peritoneal bulge that forms during the third month of gestation, prior to the descent of the testicle.

After testicular descent is complete, the processus vaginalis obliterates, and the distal portion adjacent to the testis becomes the tunica vaginalis. This process of obliteration may occur postnatally, and failure to obliterate creates an open internal inguinal ring and a patency of the processus vaginalis through which abdominal organs or tissue (if the opening is large) or fluid (if the opening is small) can pass through (**Figures 5-1** and **5-2**). Peritoneal fluid flowing from the abdomen into the scrotum via a patent processus vaginalis is called a *communicating hydrocele.* The canal of Nuck in girls is the analogous structure to the male patent processus vaginalis, and it is an extension of the peritoneum into the labia majora. Similar to boys, this canal should obliterate. Its persistence leads to an inguinal hernia in girls.

Incidence

One percent to 5% of children will develop inguinal hernias. Risk factors include male sex (boys are 5–10 times more likely to develop inguinal hernias than girls), low birth weight (<1,500 g), and preterm birth (up to 30% of patients born prematurely will develop inguinal hernias). About one-third of all inguinal hernias manifest prior to 6 months of age, and most manifest by 3 to 4 years of age. Bilateral inguinal hernias occur in up to 20% of patients, although up to 60% of patients with

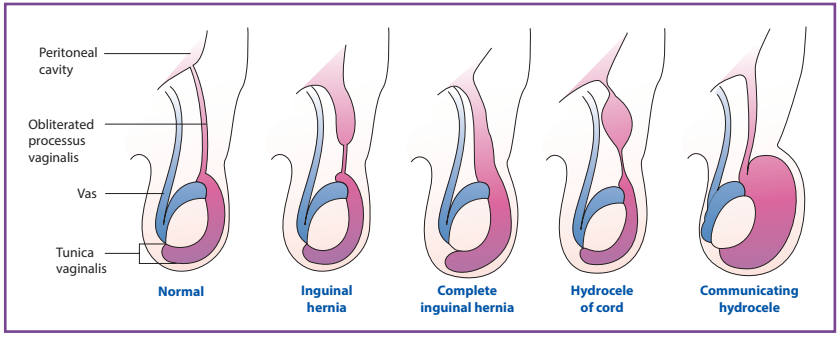

Figure 5-1. Anatomy of inguinal hernia and hydroceles. Depending where and how completely the processus vaginalis obliterates, a hydrocele of the cord or hernia can develop that tracks only in the groin or all the way to the scrotum.

Reprinted with permission from Palmer LS. Scrotal swelling and pain. In: McInerny TK, Adam HM, Campbell DE, DeWitt TG, Foy JM, Kamat DM, eds. *American Academy of Pediatrics Textbook of Pediatric Care.* 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2017:1575.

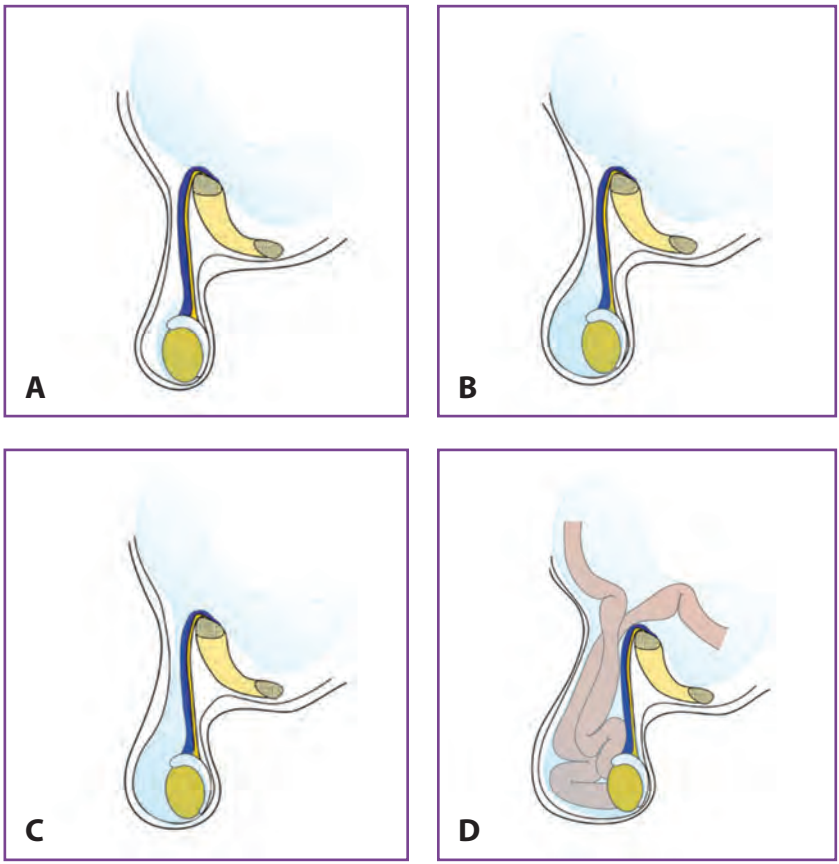

Figure 5-2. Schematic representation of inguinal canal, hydroceles, and hernias. **A,** Normal anatomy of spermatic cord and inguinal canal. **B,** Scrotal hydrocele results from fluid around the testis within the tunica vaginalis; in this image, the processus vaginalis has obliterated. **C,** Communicating hydrocele exists when the processus vaginalis is patent through the inguinal canal. **D,** Herniation of bowel into the scrotum in an inguinal hernia. Images courtesy of Paul Gleich, MD.

unilateral hernias are found to have a contralateral patent processus vaginalis when explored.

Studies have shown a genetic predisposition to inguinal hernias, with 20% to 28% of patients having a positive family history. While most inguinal hernias are an isolated finding, they have been found to be associated with more than 200 syndromes or conditions, including cryptorchidism, disorders of sex differentiation, bladder exstrophy,

epispadias, prune-belly syndrome (ie, Eagle-Barrett syndrome), posterior urethral valves, Ehlers-Danlos syndrome, cystic fibrosis, and Marfan syndrome (**Table 5-1**). Additional risk factors for development of an inguinal hernia are presence of a ventriculoperitoneal shunt, peritoneal dialysis, and abdominal ascites (which can lead to increased abdominal pressures that force abdominal fluid or contents through a patent processus vaginalis).

Table 5-1. Risk Factors for Increased Incidence of Hernia in Infants and Children

Type	Risk Factor
Urogenital factors	Undescended testis Bladder exstrophy, epispadias Prune-belly syndrome Disorders of sex development Posterior urethral valves
Increased peritoneal fluid	Ascites Presence of ventriculoperitoneal shunt Peritoneal dialysis
Increased intra-abdominal pressure	Severe ascites (liver failure) Repair of gastroschisis, exomphalos Meconium peritonitis Severe constipation
Pulmonary issues	Cystic fibrosis
Connective tissue disorders	Ehlers-Danlos syndrome Marfan syndrome Mucopolysaccharidosis
Skeletal factors	Development dysplasia of hip

Adapted from Singal AK, Shukla AR. Pediatric inguinal hernia and hydrocele. In: Wilcox D, Godbole P, Cooper C, eds. *Pediatric Urology Book*. http://www.pediatricurologybook.com/inguinal_hernia.html. Accessed October 16, 2018.

Outcome and Prognosis

All inguinal hernias, when diagnosed, require surgical repair (see the Surgical Repair [Herniorrhaphy] section). Most children do well after surgery, although complications can occur in 1% to 2%, including bleeding, wound infection, recurrent hernia (0.5%–2.0%), iatrogenic injury to hernia contents or spermatic cord, postoperative hydrocele, iatrogenic acquired cryptorchidism, or testis atrophy and/or infarction (rare but more common in cases of incarceration).

Diagnosis

Inguinal hernias are diagnosed on the basis of physical examination. In most cases, a hernia manifests as a painless bulge in the groin that extends along the inguinal canal, toward and occasionally into the scrotum. Oftentimes, the inguinal bulge is only noticeable during crying or bowel movements, when intra-abdominal pressures rise. An important question to ask when compiling the history is whether or not the bulge is intermittent (changes in size over time). Intermittent or waxing and waning bulges helps to confirm an inguinal hernia from a simple scrotal hydrocele or hydrocele of the spermatic cord. A communicating hydrocele will also fluctuate because of its association with a patent processus vaginalis but will consist only of fluid and may lack the inguinal bulge, as the patent portion of the processus is usually quite narrow.

Physical examination of the neonate or non-standing infant should take place with the patient in the supine position, with inspection of the lower abdominal skin crease along the inguinal canal from an area superior and lateral to the pubic tubercle, all the way to the scrotum. Palpation should be performed gently with 1 or 2 fingers, and the extent of the bulge or swelling should be determined. The provider should try to reduce the hernia by applying gentle pressure superiorly and laterally over the bulge, which may be indicative of the presence of any abdominal structures inside the hernia. Bowel contents or bladder may be palpable in the hernia, and with reduction, the provider may notice a gurgling sound or feel the sensation of bubbles popping. In some cases, when the hernia is not obvious at examination, the provider may palpate a thicker spermatic cord when rolled over the pubic tubercle, which feels like the sensation of rubbing silk together and is thus called "the silk-stocking sign." At physical examination, the location, size,

and consistency of each testis should be noted in the male patient. Any incompletely descended or retractile testis should undergo orchiopexy (surgical fixation into the scrotum) at the time of hernia repair.

Older infants and children should be examined in the standing position. Techniques to increase intra-abdominal pressure (crying in infants; jumping, coughing, blowing balloons, or laughing in older children) can be applied in the office if the hernia is not apparent. In the era of smartphones, astute parents or guardians may bring a picture of the bulge to the office visit (**Figure 5-3**).

Any hernia that cannot be reduced during physical examination is considered incarcerated, and the patient should be referred immediately to an emergency department. Parental education on the signs and symptoms of hernia incarceration, including irritability or the inability to console the child, a persistent or larger bulge that does not go away spontaneously or with gentle manually pressure, decreased or loss of appetite, abdominal distention, vomiting, and lack of stool, is critical at each provider encounter. The parent or guardian with concern for incarceration should be counseled to bring the child to the emergency department immediately.

Figure 5-3. A photograph taken with a smartphone by a parent to capture the inguinal bulge and confirm the presence of inguinal hernia.

Evaluation

Imaging

Imaging studies are unnecessary in most cases because the diagnosis is based on history, parental reporting, and physical examination. When ultrasonography (US) is performed, it may be used to identify an echolucent area in the groin that extends anteromedially to the spermatic cord or a piece of omentum or even peristaltic bowel (**Figure 5-4**). If a large hydrocele component is limiting palpation of the ipsilateral testicle, US may help identify the presence and health of the testicle. Rarely, a hernia (often only in cases of incarceration) may compromise blood flow to the testis by placing significant pressure on the spermatic cord. In these cases, Doppler US may be needed to confirm testicular blood flow. No blood tests or other studies are recommended for the typically developing infant or child with an inguinal hernia.

Differential Diagnosis

The differential diagnosis of the inguinal hernia includes hydrocele of the spermatic cord, simple hydrocele, lipoma of the spermatic cord, testicular torsion, undescended testis, torsion of a testicular or epididymal

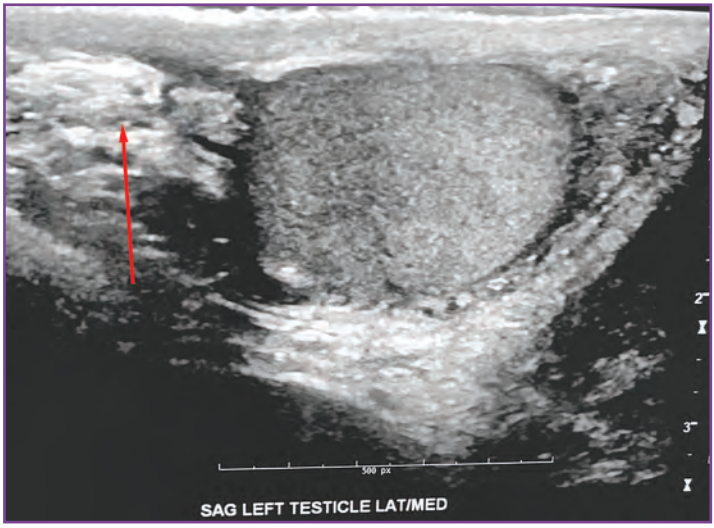

Figure 5-4. Ultrasonographic image of inguinal hernia containing omentum and bowel (arrow).

appendage, hematocele (ie, blood within the tunica vaginalis around the testis, often after trauma), epididymitis or orchitis, varicocele, testicular tumors, paratesticular tumors, femoral artery aneurysm, or lymphadenopathy (**Table 5-2**).

Table 5-2. Differential Diagnosis for Inguinal Hernia

Type	Differential Diagnosis
Fluid-filled structures around the testicle	Simple hydrocele Hematocele
Testicular process	Testicular torsion Torsion of testicular appendage Orchitis Undescended testicle Testicular tumor
Epididymal process	Epididymal cyst Torsion of epididymal appendage Epididymitis
Spermatic cord process	Hydrocele of spermatic cord Lipoma of the spermatic cord Varicocele Paratesticular tumor
Other	Femoral artery aneurysm Lymphadenopathy

Inguinal hernia, in most cases, can be distinguished from other diagnoses on the basis of physical examination findings: The hernia sac should start at the internal inguinal ring, and content should be reducible with gentle pressure. A communicating hydrocele is also a result of a patent processus vaginalis but does not contain the abdominal contents, as described earlier. (This will be discussed in the Hydrocele section.) A simple scrotal hydrocele is often misdiagnosed as an inguinal hernia in young infants and leads to referral to a surgeon. A scrotal hydrocele may extend to the internal ring but may be distinguished from a hernia or communicating hydrocele in that it does not intermittently swell

and will often be quite firm, even without the pain or discomfort of an incarcerated hernia. US may assist in confirming the diagnosis via lack of a patent processus vaginalis (**Figure 5-5**).

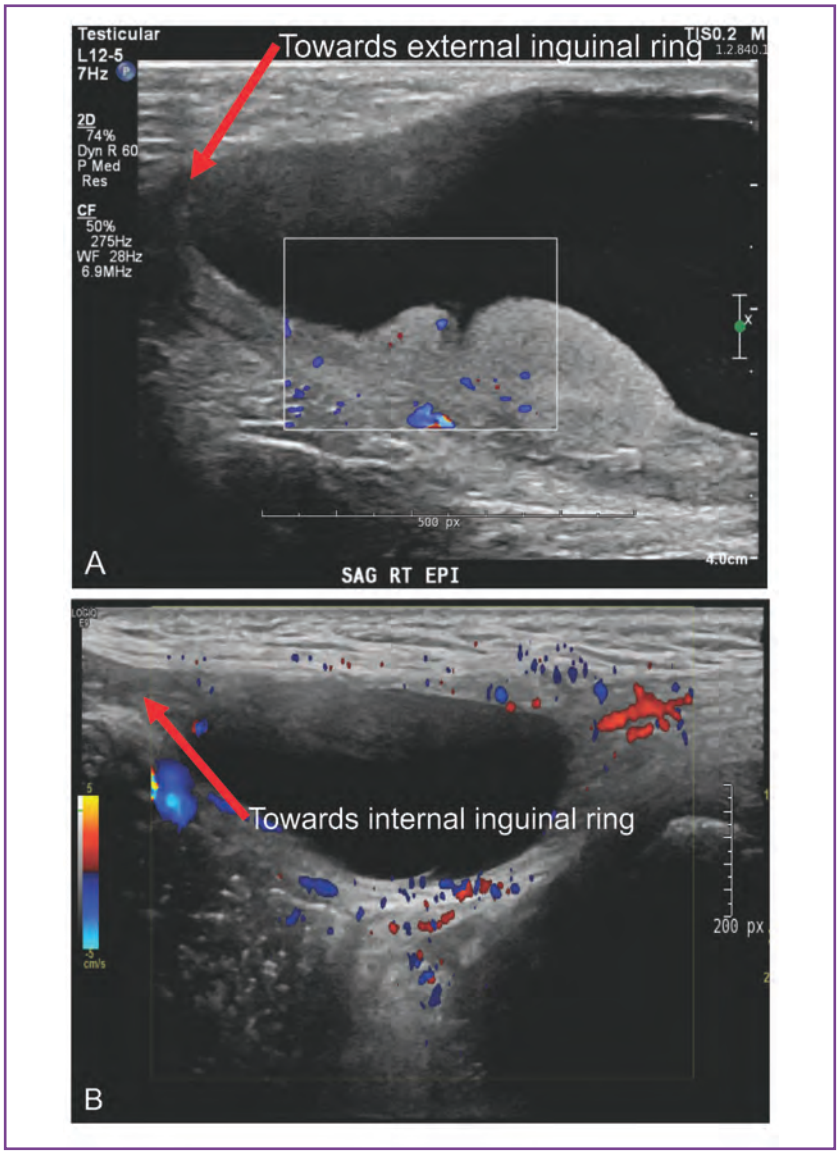

Figure 5-5. A, Ultrasonographic image of a large, simple hydrocele extending from the scrotum into the inguinal canal. **B,** In some cases, the hydrocele can be noted to extend all the way to the internal inguinal ring.

Treatment Options and Outcomes

Surgical Repair (Herniorrhaphy)

All inguinal hernias require surgical repair and should be referred to a pediatric surgical specialist. Timing of surgery is most often elective but is usually performed shortly after diagnosis (within several weeks), especially in neonates and infants. If the hernia becomes incarcerated (ie, unable to be reduced) with or without strangulation (ie, the blood flow to herniated tissue or an organ is blocked), surgical correction should be performed emergently. An initial attempt at manual reduction may be performed by the appropriate specialist in the emergency department prior to surgical repair. Even if reduction is successful, surgery is still indicated at that encounter. Strangulation can lead to necrosis of the hernia contents, which may be omentum, bowel, bladder, or any other abdominal organ.

The traditional surgical approach to the indirect inguinal hernia is high ligation of the hernia sac at the internal inguinal ring. This technique is most often performed via an inguinal incision and has a high success rate, low morbidity, and good cosmesis. Laparoscopic hernia repair is preferred by some, although studies suggest a slightly higher risk of recurrence (4%) when compared to open repair. Proposed advantages to laparoscopy include the ability to bypass cord structures with lower risk of iatrogenic injury, direct visual control of bowel reduction, and ability to visualize the contralateral internal inguinal ring for patency.

A unilateral hernia is associated with a contralateral patent processus vaginalis in up to 60% of cases, although the true risk of a patent processus vaginalis or open internal inguinal ring regarding future hernia development is unknown. For this reason, contralateral exploration or assessment of the contralateral internal inguinal ring is controversial in unilateral cases. The incidence of a contralateral patent processus vaginalis is inversely proportional to age, with the greatest risks occurring in neonates and infants. Any child with unilateral inguinal hernia and an additional risk factor for development of an inguinal hernia (eg, presence of ventriculoperitoneal shunt, need for peritoneal dialysis, abdominal ascites) should undergo contralateral exploration and repair of an identified patent processus vaginalis or open internal inguinal ring. The decision to explore the contralateral inguinal region or to laparoscopically assess the contralateral internal inguinal ring is

dependent on the age of the patient, additional comorbidities, and surgeon preference, after discussion of risks and benefits with the patient's parents or guardians.

While most patients do well after surgical repair, complications may occur in 1% to 2% of cases. Early postoperative complications include bleeding and wound infection, which are rare (<2%). The most common intermediate or long-term complication is recurrent inguinal hernia, which occurs in 0.5% to 1% of patients after an uncomplicated repair but at higher rates after incarceration and after repair in preterm neonates and infants (2%–6%). Recurrent inguinal hernias require repeat surgical repair. Other rare complications include iatrogenic or acquired cryptorchidism (ie, a previously descended testis that is found to no longer be in the scrotum), testicular atrophy and/or infarction (also more common in cases of incarceration), postoperative hydrocele, and injury to the vas. Postoperative hydroceles should be observed for 1 year for spontaneous resolution. If spontaneous resolution does not occur, surgical correction is often necessary.

When to Refer

All pediatric patients with inguinal hernias should be referred to a pediatric surgical specialist, such as a pediatric urologist or pediatric surgeon. Any patient suspected of having an incarcerated hernia should be referred to the emergency department immediately.

Clinical Pearls

- All pediatric patients with hernias require referral to a pediatric surgical specialist.
- Parents or guardians may be asked to take a picture of the inguinal bulge if it is not evident at physical examination in the office.
- Signs and symptoms of incarcerated hernia include irritability or the inability to console the child, a persistent or larger bulge that does not go away spontaneously or with gentle manual pressure, decreased or loss of appetite, abdominal distention, vomiting, and lack of stool.
- Parental education on signs and symptoms of inguinal hernia incarceration is of critical importance at each provider encounter.
- Incarcerated hernias are surgical emergencies and require an attempt at manual reduction in the emergency department, followed by immediate surgical repair.

- Annual scrotal examinations after inguinal hernia repairs are important to monitor the patient for iatrogenic or acquired cryptorchidism, as well as checking for testicular hypotrophy and hernia recurrence.

Hydrocele

Introduction

Pathophysiology

As described earlier in the Hernia section, the processus vaginalis forms as a peritoneal extension or bulge, from the abdominal cavity through the inguinal canal into the scrotum. This communication normally spontaneously obliterates after testicular descent is complete.

The term *hydrocele* can be used to describe several entities (see **Figure 5-1**). A *simple scrotal hydrocele* is fluid contained within the tunica vaginalis that surrounds the testis without communicating proximally (ie, the processus vaginalis is not patent) (see **Figures 5-1** and **5-2**). This can be left over from birth or result from testicular inflammation or irritation, resulting in fluid secretion, or it can be idiopathic. A *hydrocele of the spermatic cord* is fluid contained within a segment of patent processus vaginalis, with obliterated processus distally and proximally. A *communicating hydrocele* is fluid within the tunica vaginalis surrounding the testis, along with a patent processus vaginalis that is only large enough to allow peritoneal fluid through (see **Figures 5-1** and **5-2**).

Incidence

Most new hydroceles that develop after birth and before puberty are communicating with a patent processus vaginalis. In fact, studies show that more than 80% of boys undergoing hydrocele repair have communicating hydroceles. Simple noncommunicating scrotal hydroceles are most common in neonates, spontaneously resolve during infancy, and often do not require surgery. Those that appear during or after puberty are also more likely to be noncommunicating simple scrotal hydroceles. Preterm birth and low birth weight are risk factors for hydroceles.

Diagnosis

As with inguinal hernia, the diagnosis of a hydrocele is based on physical examination findings in relation to history, as supplied by the parents or guardians. Most hydroceles manifest as painless masses. Simple hydroceles, however, can be a result of inflammation and may have a characteristic history of pain or trauma that should be queried. A communicating hydrocele can be differentiated from a true simple scrotal hydrocele on the basis of fluctuation in size over the course of a day or weeks. The size of a communicating hydrocele waxes and wanes, due to fluid going back and forth through the patent processus vaginalis. While the scrotal hydrocele should remain stable in size, it may resolve over time. A hydrocele of the spermatic cord also usually manifests as a painless mass superior to and separate from the testicle and may be large or small but is usually stable in size over time.

Physical examination should be performed as described earlier in the Hernia section, and all pediatric patients with a hydrocele should be examined thoroughly for a bowel containing inguinal hernia. The provider should gently apply pressure on the hydrocele to see if it can be decompressed or if the size changes, which indicates a patent processus vaginalis. One must be careful not to confuse a hydrocele of the spermatic cord with a testis, as the two can be similar in size and shape. The fluid in a hydrocele may have a bluish hue through the scrotal wall and should transilluminate when a bright light (ie, a flashlight) is held up against it. Neonatal bowel may also transilluminate, so care must be taken in performing a complete and detailed physical examination. If the testis is palpable, its size, consistency, and location should be documented.

Evaluation

Imaging

As with hernia, radiologic imaging studies have a minimal role in the diagnosis of hydroceles. Scrotal US can help identify the presence and health of a nonpalpable testicle surrounded by hydrocele fluid and confirm the presence of simple hydrocele fluid if there is concern at physical examination. In addition, it can help distinguish a hydrocele of the cord from other paratesticular masses if there is any concern at examination.

Differential Diagnosis

The differential diagnosis for hydrocele is similar to that for inguinal hernia and includes lipoma of the spermatic cord, testicular torsion, undescended testis, torsion of a testicular or epididymal appendage, hematocele (ie, blood within the tunica vaginalis around the testis, often after trauma), epididymitis or orchitis, varicocele, testicular tumors, paratesticular tumors, femoral artery aneurysm, and lymphadenopathy.

Outcome and Prognosis

Resolution

Both communicating and simple scrotal hydroceles in infants have the potential to resolve spontaneously, within the first 2 years after birth (range of 60%–85% by 18 months in published observational series). Communicating hydroceles may resolve if the processus vaginalis obliterates postnatally (usually in the first year after birth), and noncommunicating simple scrotal hydroceles resolve as the fluid in the tunica vaginalis space is reabsorbed. If a hydrocele grows or persists more than 1 year after birth, referral to a pediatric surgical specialist is warranted for surgical correction. Hydroceles of the spermatic cord rarely resolve spontaneously and should also be surgically repaired after 1 year of age.

Surgery

Children older than 1 year with a persistent or new onset of hydrocele should undergo surgical repair. Children younger than 1 year can undergo repair if their hydrocele is progressively increasing in size. If a communicating hydrocele is suspected or if the child is prepubertal, an inguinal incision and high ligation of the patent processus vaginalis at the level of the internal inguinal ring is the standard of care. In postpubertal boys or men without clinical suspicion for a communicating hydrocele, a trans-scrotal approach for simple hydrocele repair and excision is preferred. However, the surgeon might have to make an inguinal incision if a patent processus is found.

Most pediatric patients do well after surgery with rare complications seen, such as bleeding, infection, recurrent hydrocele, and iatrogenic injury to the testis or spermatic cord structures. Hydroceles can rarely recur or persist, and repeat surgery may be required.

When to Refer

- Refer the patient to a pediatric surgical specialist if a communicating hydrocele persists beyond 1 year of age or is enlarging.
- Any neonate suspected of having a communicating hydrocele can be observed initially. Refer sooner if inguinal bulging is noted or is enlarging.
- If simple scrotal hydrocele persists after 1 year of age, refer the patient to a pediatric surgical specialist.
- Children older than 1 year with any newly developed hydroceles should be referred to a specialist.

Clinical Pearls

- *Hydrocele* can refer to one of several anatomically distinct entities.
- A communicating hydrocele (ie, patent processus vaginalis) can be differentiated from an isolated simple scrotal hydrocele on the basis of fluctuation in size and should be treated as an inguinal hernia.
- Simple scrotal hydroceles in infants have the potential to resolve spontaneously and should be observed for 1 year prior to surgical intervention.
- Hydroceles of the spermatic cord can be confused with the ipsilateral testis and can also be observed for 1 year prior to surgical intervention.

Varicocele

Introduction

A *scrotal varicocele* is an abnormal dilation and tortuosity of the internal spermatic veins in the pampiniform plexus, located within the spermatic cord (see **Figure 5-2**). Varicocele is a common finding in adolescent boys and a common reason for referral to the pediatric urologist. While uncommon in prepubertal boys, the prevalence of varicocele increases during adolescence to approach the incidence rate of approximately 15% in adult men.

Incidence

Given the asymptomatic nature of most pediatric varicoceles, the true incidence of varicoceles in pubertal boys is difficult to estimate. Population-wide screening studies among school-aged boys indicated

that varicoceles occur in fewer than 1% of boys younger than 11 years, 8% of boys 11 to 14 years of age, and 14% to 16% of boys 15 to 19 years of age. Most varicoceles (>90%) occur on the left and bilaterally, with isolated right-sided varicoceles in the pediatric population occurring infrequently (approximately 5% of cases). Risk factors for varicoceles include increased height, low body weight, and low body mass index. There is no predilection for race or ethnicity. Genetic susceptibility likely plays a large role in varicocele risk, since 67% of the sons of an affected father will also develop varicoceles.

Pathophysiology

The pathophysiology of the varicocele is likely multifactorial. The anatomic differences in venous return between the left and right spermatic veins are thought to play a key role in the higher incidence of varicoceles on the left, as compared to the right side. The more vertical and longer left testicular vein is hypothesized to have a larger column of standing blood and, thus, a higher hydrostatic pressure. While the right spermatic vein drains directly into the inferior vena cava, the left spermatic vein drains into the left renal vein. Valvular incompetence of the left internal spermatic vein at its junction with the left renal vein is hypothesized to play a role in varicocele formation.

There is evidence from multiple studies that a varicocele can alter testicular growth, spermatogenesis, and fertility potential. The specific mechanism for testicular insult or damage from varicoceles is unknown, but it is hypothesized that hyperthermia (higher temperatures secondary to poor venous return) plays a role.

Outcome and Prognosis

While an asymptomatic varicocele may seem to be of little to no concern, the fact that 20% of men with varicoceles have problems with fertility is concerning, but predicting which adolescents will become part of this 20% is more complex. Varicoceles may be associated with testicular asymmetry, scrotal pain, hormonal dysfunction, and/or abnormal semen parameters. While some varicoceles will improve over time with active surveillance, others may be associated with worsening testicular asymmetry or semen parameters. Unfortunately, prognostic indicators are largely unknown; thus, indications for varicocele repair are controversial and are evolving as more information becomes available.

Diagnosis

Most pediatric varicoceles are asymptomatic and are detected by the health care provider during physical examination at routine annual visits. Less commonly, the patient may notice the abnormality during testicular self-examination or complain of a "heaviness" or vague hemiscrotal discomfort. In rare cases, the patient may have a sharp pain that radiates to the inguinal area or that is worse while sitting or standing. The provider should perform a thorough physical examination by using various patient positions and conducting the examination in a warm room, for easier examination of the scrotum and spermatic cord. First, the scrotum should be inspected for asymmetry and for any visually obvious protruding dilated veins. Next, with the patient in the supine position, the scrotum and contents are palpated both at rest and during the Valsalva maneuver. Decompression of the varicocele when the patient is relaxed and positioned supine should be documented. Finally, the patient should be asked to stand upright, and inspection and palpation should be repeated both at rest and during the Valsalva maneuver. Classically, the dilated veins of the varicocele are described as feeling like a "bag of worms" in the scrotum (**Figure 5-6**). Smaller

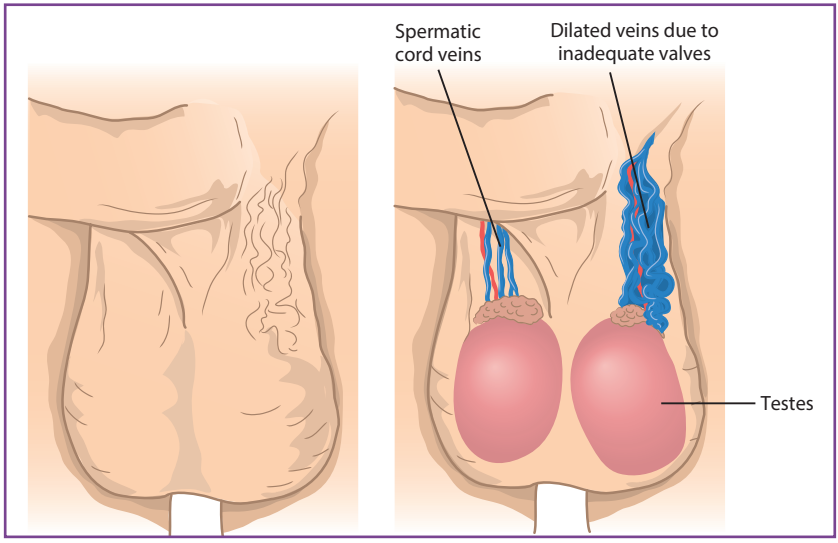

Figure 5-6. A varicocele is composed of veins with inadequate valves, which can appear as a tortuosity on the scrotum.

varicoceles may only be apparent during standing; thus, examination in both positions is essential. Varicoceles are graded on a scale of 1 to 3:

- Grade 1: Varicocele only palpated during the Valsalva maneuver
- Grade 2: Varicocele palpated without the Valsalva maneuver
- Grade 3: Large varicocele detected by visually inspecting the scrotum

However, varicocele grade has not been proven to be a consistently reliable indicator of testicular atrophy, asymmetry, abnormal semen parameters, or future fertility.

Another key aspect of the examination is not simply identifying the varicocele but evaluating the testicles themselves. Testicular size is a surrogate for testicular health and is used as one indicator of potentially clinically significant varicocele. Measurement of testicular volumes is important in determining volume discrepancies between the testicle on the ipsilateral side and the contralateral testicle. Methods for measuring testicular volume include the use of orchidometers, calipers, or US. Orchidometry is practical in the office setting and offers a quick and inexpensive means to determine testicular volume. The Prader orchidometer uses a string of ovoid-shaped beads, while the Takihara rings are plastic cards with punched-out ellipses of increasing sizes, allowing estimation of the testicular volume (**Figure 5-7**).

When calipers or US are used to measure testicular diameters, the most common accepted equation is the Lambert formula (**Figure 5-8**): Testicular volume (in milliliters) = length (cm) × width (cm) × height (cm) × coefficient of 0.71. US is considered the most sensitive test for testicular asymmetry. When using the percentage of asymmetry between the affected (usually left) and unaffected (usually right) testis, the cutoff for determining which boys are at risk for future problems and thus require an intervention is controversial. Partially contributing to the difficulty in interpreting size discrepancy is the normal asymmetrical growth of the testicles at puberty. Arbitrary values of 10%, 15%, and 20% have been the most common values used in the literature, and recent data have suggested an association between increasing percentage of asymmetry and worse semen parameters.

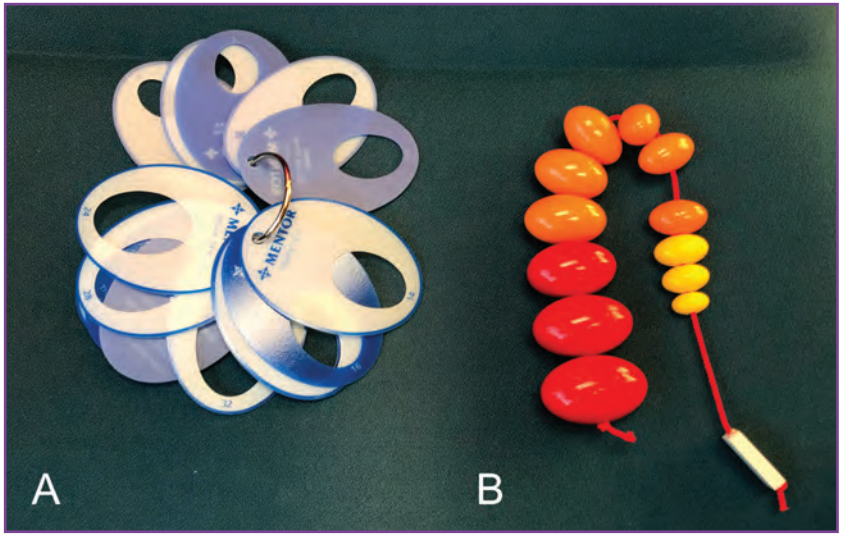

Figure 5-7. Two methods of estimating testicular volume during the physical examination include (**A**) the Takihara ring orchidometer, which involves the use of plastic cards with punched-out ellipses of increasing sizes, and (**B**) the Prader orchidometer, which is a string of ovoid-shaped beads.

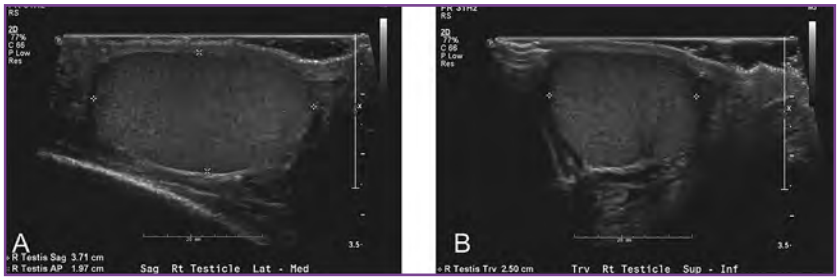

Figure 5-8. Ultrasonography can be used to obtain the testicular volume by measuring the testis in 3 dimensions: (**A**) length, width, and (**B**) depth or height. These diameters can then be used in the Lambert formula to calculate testicular volume in milliliters: length (cm) × width (cm) × height (cm) × coefficient of 0.71.

Evaluation

Imaging and Laboratory Studies

While physical examination is the standard of reference for diagnosis, some pediatric urologists advocate for scrotal Doppler US to confirm the diagnosis of equivocal physical examination findings, measure

testicular volumes, and/or help guide management (**Figure 5-9**). Additional imaging or laboratory studies are not routinely recommended for adolescent boys with traditional presentations of varicoceles. Evaluation of the retroperitoneum for masses with US or computed tomography in boys with *(a)* solitary right-sided varicoceles that do not decompress when the child is supine and relaxed and *(b)* sudden onset of unilateral or bilateral varicoceles is controversial, although recommended by some authors.

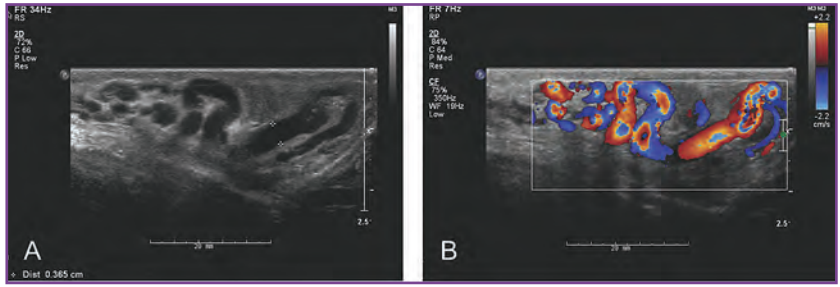

Figure 5-9. Ultrasonographic images of a left grade 3 varicocele without Doppler imaging (**A**) and with Doppler imaging (**B**).

Some studies have documented abnormal response to gonadotrophin-releasing hormone stimulation in boys with varicoceles, although the significance of this finding is unknown. Semen analysis can help guide treatment and should be performed in all cases when possible (Tanner stage >5, family and patient accepting).

Differential Diagnosis

When a varicocele is detected or suspected, other scrotal and testicular pathologic findings should be ruled out, and the differential diagnosis should include hydrocele, spermatocele, inguinal hernia, testicular mass, spermatic cord mass, and lipoma.

Treatment Options and Outcomes

Observation or active surveillance is the most appropriate choice for most adolescent boys with varicoceles, unless a surgical indication is present. Indications for the treatment of adolescent varicoceles varies at this time, and studies to elucidate the timing and need for surgical intervention and optimal treatment are under investigation. Ideally, any

indication for treatment should address the presence of symptoms and have bearing on future paternity, and a varicocele repair should reverse negative parameters ostensibly caused by the presence of a varicocele. Unfortunately, it is difficult to evaluate the potential long-term harm of an adolescent varicocele; thus, surrogate markers or indicators are used. Both the American Urological Association (AUA) and the American Society for Reproductive Medicine (ASRM) in their best practice policies give 2 indications for varicocele treatment: *(a)* objective evidence of reduced ipsilateral testicular size, or *(b)* semen abnormality. Interestingly, no cutoff for testicular hypotrophy or specific values for abnormal semen parameters are given, reflecting the conflicting data in the literature as described previously. It is important to note that transient testicular asymmetry may occur during puberty in children without varicoceles. Therefore, some providers will follow up with a child who has a varicocele and testicular asymmetry for several years to determine if it is persistent before offering surgical intervention. In its guideline, the European Association of Urology recommends varicocele repair in adolescents with *(a)* an associated small testis, *(b)* an additional testicular condition that is affecting fertility, *(c)* bilateral palpable varicocele, *(d)* pathologic sperm quality, and *(e)* symptomatic varicocele (ie, discomfort or pain).

Active Surveillance

Adolescents undergoing observation should undergo physical examination every 1 to 2 years, depending on provider and institution preference. Repeat scrotal Doppler US may be performed at the discretion of the provider. A semen analysis should be performed when clinically appropriate.

Surgical Repair (Varicocelectomy)

All surgical approaches to varicocele repair are based on ligation of the spermatic veins and differ on the basis of the location at which the veins are exposed. Most common techniques for varicocelectomy include open abdominal retroperitoneal and suprainguinal (Palomo), open inguinal, open subinguinal, and laparoscopic suprainguinal or retroperitoneal approaches. Microscopy can be used with the inguinal, subinguinal, and even retroperitoneal approaches. The most important factors when choosing a technique are surgeon experience and

preference and complication rates. Alternatives to surgical repair include radiographic embolization and antegrade or retrograde sclerotherapy.

Postoperative complications include bleeding, hematocele, wound infection, varicocele recurrence (0%–30%, depending on technique), hydrocele (0%–30%; lower for microscopic subinguinal technique), and genitofemoral nerve injury (seen in 7% of patients after laparoscopic varicocelectomy; usually resolves spontaneously). While most patients (70%–80%) experience catch-up growth (ie, the affected testicle grows to become similar in size to the unaffected testicle) after varicocelectomy, rare cases of testicular atrophy have been documented.

Postoperative follow-up includes annual or biannual physical examination for assessment of testicular size, catch-up growth, varicocele recurrence, symptoms, and hydrocele formation.

When to Refer

All pediatric patients with clinically evident varicoceles or suspicion for varicocele should be referred to a pediatric urologist for further evaluation and management.

Clinical Pearls

- While uncommon in prepubertal boys, the prevalence of varicocele increases during adolescence to approach the incidence rate of approximately 15% in adult men.
- Varicocele can alter testicular growth, spermatogenesis, and fertility potential.
- Semen analysis can help guide treatment and should be performed in all cases when possible (Tanner stage >5, family and patient accepting).
- Observation or active surveillance is the most appropriate choice for most adolescent boys with varicoceles, unless a surgical indication is present.
- In their best practice policies, both the AUA and the ASRM give 2 indications for varicocele treatment: *(a)* objective evidence of reduced ipsilateral testicular size or *(b)* semen abnormality. Peripubertal boys may have asymmetrical testicular growth as part of puberty, which can confuse the use of testicular volume as an indication for treatment.

Testicular Cysts

Introduction

Simple testicular cysts are rare and may occur in the tunica albuginea, tunica vaginalis, rete testis, or testicular parenchyma. The differential diagnosis of the intra- and extratesticular cystic lesion is large, but most lesions in the prepubertal boy are benign. Despite scant literature on the true incidence rates of testicular cysts, the most common intratesticular cyst is thought to be the benign epidermoid cyst.

Diagnosis

Intra- and extratesticular cystic lesions are most commonly diagnosed on the basis of physical examination findings of unilateral testicular enlargement, increased testicular firmness, or palpable painless mass. The lesions may also be identified on images obtained for scrotal pain or for other reasons. A complete physical examination should be completed, and evidence of precocious puberty or normal postpubertal changes should be recorded.

Evaluation

Imaging and Laboratory Studies

Scrotal US with Doppler is the first-line imaging modality for scrotal masses or lesions. US can help characterize the lesion on the basis of location, size, consistency, presence of cystic components, and areas of calcification or blood flow. In addition, US can be used to visualize the normal areas of the testis if the lesion is localized, as well as the epididymis and contralateral testis and epididymis. An epidermoid cyst at US has the classic appearance of hyperechoic and hypoechoic rings or "onion skin," with no internal blood flow (**Figure 5-10**). A benign teratoma, the most common prepubertal primary testicular tumor, is commonly seen as a heterogeneous mass with areas that are solid, cystic, and/or calcified.

When the provider is concerned for a testicular or paratesticular neoplasm, serum biomarkers should be obtained, including human chorionic gonadotropin-β and α-fetoprotein levels. Postpubertal patients

Figure 5-10. An epidermoid cyst is a benign lesion that can be identified at ultrasonography by the classic appearance of hyperechoic and hypoechoic rings or "onion skin," with no internal blood flow.

with intratesticular cystic lesions that are concerning for malignancy should be treated as adults in terms of evaluation and treatment, since most testicular lesions and masses in this population are malignant tumors (see Chapter 12, Urological Oncology in Pediatrics).

Cystic dysplasia of the rete testis is rare but may be associated with ipsilateral renal agenesis; therefore, some authors recommend renal US in these patients. On scrotal US images, this malformation appears as cystic lesions localized to the upper pole of the testis (**Figure 5-11**).

Differential Diagnosis

Intra- and extratesticular cysts have a broad differential diagnosis. For a cyst found within the testis itself, this differential includes epidermoid cyst, dermoid cyst, teratoma, cystic dysplasia of the rete testis, simple cyst, juvenile granulosa cell tumor, testicular cystic lymphangioma, cystic degeneration after testicular torsion, ovotestis, testicular dysgenesis, trauma, and testicular tumors. While most testicular tumors are solid, they can have cystic components—especially choriocarcinomas and tumors associated with necrosis or hemorrhage. The rare Leydig cell tumor may be suspected on the basis of a small intratesticular lesion combined with physical changes (ie, precocious puberty secondary to

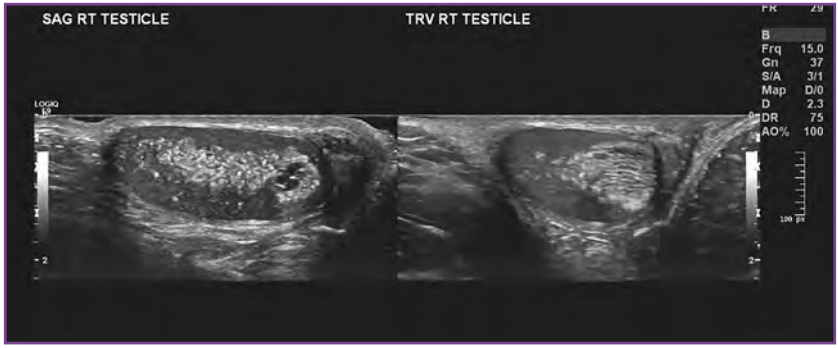

Figure 5-11. Ultrasonographic images of cystic dysplasia of the right rete testis in a 2-year-old boy with a history of right multicystic dysplastic kidney and recent "scrotal swelling."

increased testosterone levels—pubic or facial hair, enlarging of testis and penis, and acne) consistent with a Leydig cell tumor.

The differential diagnosis of extratesticular cystic lesions includes epididymal simple cyst, hydrocele, spermatocele, torsion of a testicular or epididymal appendage, varicocele (can be differentiated from cystic lesions on the basis of Doppler blood flow), inguinal hernia, cryptorchidism, trauma, and paratesticular tumors. Paratesticular tumors that should be included in any differential diagnosis for an extratesticular lesion include adenomatoid tumor (usually in older patients >20 years of age), papillary cystadenoma, lipoma, and rhabdomyosarcoma.

Spermatoceles, or epididymal cysts, are a common source of referral to urologists. They most often occur in the upper pole of the epididymis and are variable in size. At physical examination, they are characteristically easily felt to be separate from the testis and are moveable. When found in postpubertal boys, these are called *spermatoceles* because they are commonly filled with sperm. Scrotal US allows them to be readily distinguished from other entities (**Figure 5-12**). They have little clinical significance, are almost always asymptomatic, occur postpubertally after the start of sperm production, and rarely require removal.

Treatment Options and Outcomes

Specific treatment depends on the characteristics of the cystic lesion, including size, growth, and appearance. Most cystic lesions in prepubertal boys are benign in nature, will have negative preoperative tumor markers (α-fetoprotein and β-human chorionic gonadotropin levels),

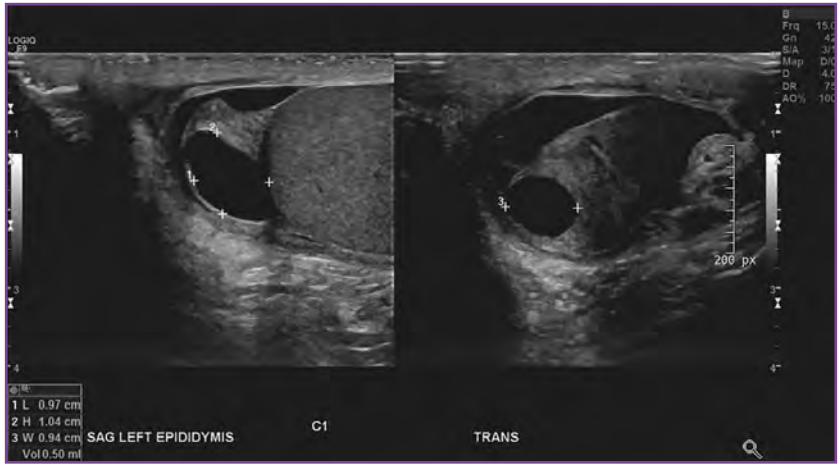

Figure 5-12. Ultrasonographic images of spermatocele in a 15-year-old boy with a scrotal mass palpated at his annual visit to his primary care physician.

and can be managed with a testicular sparing partial orchiectomy (ie, excision of the cyst while leaving the remainder of the testis intact). The surgical approach should be through an inguinal incision, with delivery of the testis through this incision and at the time of surgery; biopsy samples of the cystic lesions and adjacent areas can be sent to the pathology department for intraoperative diagnosis to help guide treatment. A total orchiectomy (ie, removal of the entire testis) is the standard of care if there is any concern for malignancy, especially in a postpubertal child, but this is rare in the prepubertal period. Cystic dysplasia of the rete testis is often treated with partial orchiectomy, although more recently, authors have recommended observation or active surveillance.

Management of extratesticular cystic lesions depends on the location and appearance of the lesion. Simple epididymal cysts or spermatoceles (in postpubertal boys) can be observed over time for signs of growth or can be excised, if they are causing symptoms such as pain. Any lesion that is concerning for tumor should be excised via an inguinal incision with appropriate workup on the basis of pathologic findings.

Outcomes after treatment depend on the specific lesion. Most prepubertal intra- and extratesticular cystic lesions are benign in nature, and patients require no further treatment or imaging surveillance after excision or partial orchiectomy. Annual scrotal examination with palpation

and characterization of each testis should be performed, as is standard for all pediatric patients.

When to Refer

All pediatric patients with testicular or extratesticular lesions, whether cystic or not, should be referred to a pediatric surgical specialist for further evaluation and management.

Clinical Pearls

- Most cystic lesions in prepubertal boys are benign.
- Referral to the pediatric surgical specialist is required for all intra- and extratesticular cystic lesions.
- The differential diagnosis for scrotal lesions and masses is long and should be kept in mind when examining all pediatric patients with lesions.
- After treatment, most patients require nothing more than annual scrotal examinations, although additional follow-up may be necessary on the basis of pathologic findings and the specific diagnosis.

Scrotal Median Raphe Cysts

Median raphe cysts are rare, benign congenital lesions of the male genitalia that occur in the midline of the perineum, anywhere from the urethra to the anus. They can present as a solitary cyst or as multiple cysts and occasionally as a string of cysts along the midline of the perineum and median raphe of the scrotum and penis (**Figure 5-13**). These cysts are believed to be the result of a defect during embryological development that results in the trapping of tissue beneath the epidermis, although the exact pathophysiology is unknown.

Most of these cysts (>75%) are asymptomatic in childhood, but they can grow over time. Clinical symptoms such as pain are more common in later adolescence and adulthood, and complications can arise from infections.

Simple excision is recommended by most authors to prevent future symptoms or infections. Complete excision is required, as these lesions can recur if a portion is left in situ. Spontaneous regression has been

Figure 5-13. Image of a male patient with median raphe cysts, manifesting as a string of cysts along the midline of the perineum and median raphe of the scrotum.

described in the literature, but, given the rarity of the disease process, little is known about the true natural history of these cysts.

When to Refer

Refer patients to the pediatric surgical specialist for all concerning cysts of the perineum, scrotum, and penis.

Testicular Microlithiasis

Testicular microcalcifications (microlithiasis) may be identified incidentally on scrotal US images in 1% to 3% of boys between 0 and 19 years of age (**Figure 5-14**). This finding is most often asymptomatic, and there is controversy in the literature about its association with testicular cancer. Routine surveillance with US is not necessary in patients without any risk factors for testicular cancer. Current recommendations are to perform routine self-examinations each month.

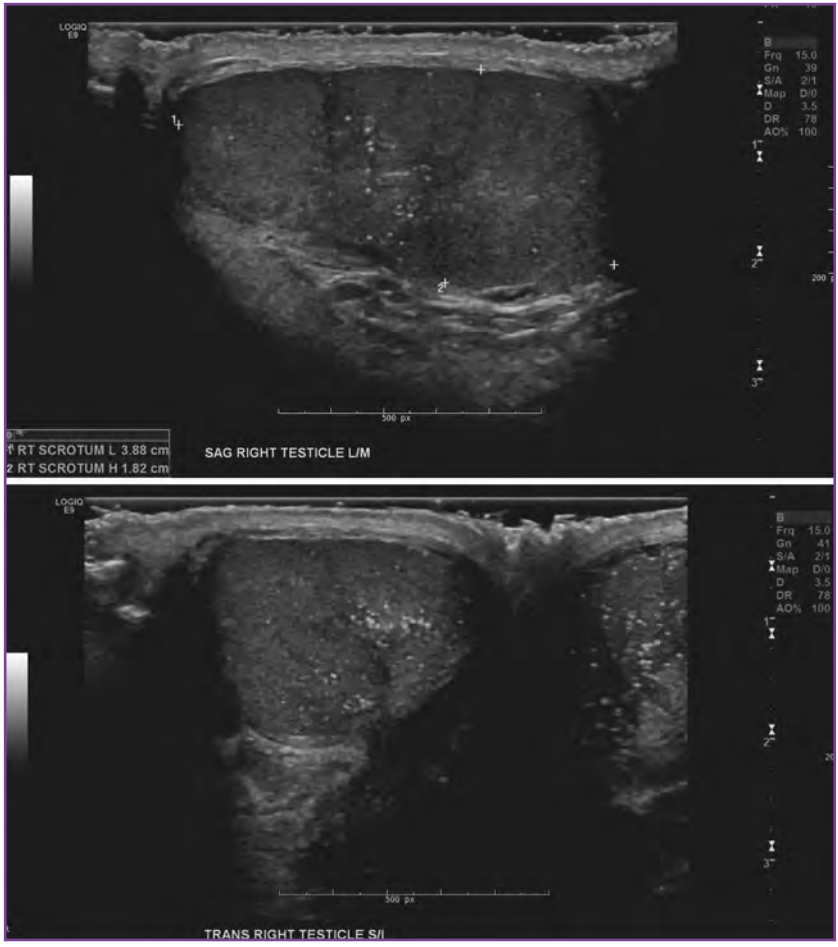

Figure 5-14. Ultrasonographic images of testicular microlithiasis.

Resources for Parents

- American Academy of Pediatrics. Inguinal hernia. HealthyChildren.org Web site. https://www.healthychildren.org/English/health-issues/conditions/abdominal/Pages/Inguinal-Hernia.aspx. Updated November 21, 2015. Accessed October 16, 2018
- American Academy of Pediatrics. Communicating hydrocele. HealthyChildren.org Web site. https://www.healthychildren.org/English/health-issues/conditions/abdominal/Pages/Communicating-Hydrocele.aspx. Updated November 21, 2015. Accessed October 16, 2018

- American Academy of Pediatrics. Varicocele. HealthyChildren.org Web site. https://www.healthychildren.org/English/health-issues/conditions/genitourinary-tract/Pages/Varicocele.aspx. Updated November 21, 2015. Accessed October 16, 2018
- Matulewicz RS, Meeks JJ. JAMA patient page. Testicular mass. *JAMA*. 2016;316(5):557. https://jamanetwork.com/journals/jama/fullarticle/2540404. Published August 2, 2016. Accessed October 16, 2018

Suggested Readings

American Urological Association Male Infertility Best Practice Policy Committee and American Society for Reproductive Medicine Practice Committee. *Infertility: Report on Varicocele and Infertility.* Linthicum, MD: American Urological Association; 2001. https://www.auanet.org/Documents/education/clinical-guidance/Varicocele-Archive.pdf. Accessed October 16, 2018

Diamond DA, Gargollo PC, Caldamone AA. Current management principles for adolescent varicocele. *Fertil Steril*. 2011;96(6):1294–1298

Hoag NA, Afshar K, Youssef D, Masterson JS, Murphy J, Macneily AE. Cystic intratesticular lesions in pediatric patients. *J Pediatr Surg*. 2013;48(8):1773–1777

Krauel L, Tarrado X, Garcia-Aparicio L, et al. Median raphe cysts of the perineum in children. *Urology*. 2008;71(5):830–831

Lao OB, Fitzgibbons RJ Jr, Cusick RA. Pediatric inguinal hernias, hydroceles, and undescended testicles. *Surg Clin North Am*. 2012;92(3):487–504, vii

Paduch DA, Skoog SJ. Diagnosis, evaluation and treatment of adolescent varicocele. *Sci World J*. 2004;4(Suppl 1):263–278

Palmer LS, Palmer JS. Management of abnormalities of the external genitalia in boys. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 11th ed. Philadelphia, PA: Elsevier; 2016:3368–3398

Tekgül S, Riedmiller H, Dogan HS, et al. *Guidelines on Paediatric Urology.* European Association of Urology. https://uroweb.org/wp-content/uploads/22-Paediatric-Urology_LR.pdf. Updated March 2013. Accessed October 16, 2018

Wang KS; American Academy of Pediatrics Committee on Fetus and Newborn, Section on Surgery. Assessment and management of inguinal hernia in infants. *Pediatrics*. 2012;130(4):768–773

CHAPTER 6

Pediatric Urinary Tract Infection

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Introduction

Incidence

Pediatric urinary tract infections (UTIs) generate a substantial disease burden in the United States. A study from the Urologic Diseases in North America Project showed that 2.4% to 2.8% of children annually seek medical care for a UTI, accounting for 1 million office visits, or 0.7% of all pediatric physician visits annually. Although outpatient management is sufficient for most children with UTIs, with fewer than 0.5% of those managed in the office necessitating subsequent admission, inpatient hospital treatment costs have been estimated at greater than $180 million per year.

Despite its prevalence, a UTI in a child can prove challenging to the clinician because of nonspecific presentation and varying potential for acute morbidity, recurrence, and long-term sequelae. This chapter relates current knowledge about the pathogenesis, evaluation, and treatment of pediatric UTIs to aid the primary care provider in creating an individualized management strategy for each child.

Definition

One obstacle providers face in the diagnosis of UTI is a lack of consensus regarding what constitutes a clinically significant UTI. Normal urine is sterile, so the presence of bacteria in the urine is a prerequisite for diagnosis. The number of colony-forming units (CFU) per milliliter sufficient for diagnosis varies according to different criteria and methods of collection, given the potential for contamination during collection. It is commonly accepted that 50,000 CFU/mL of a single uropathogenic organism are required to diagnose a UTI from a catheterized specimen, while 100,000 CFU/mL of a single uropathogenic organism are needed from a clean-catch specimen. However, the presence of bacteria in the urine alone is not sufficient to diagnose UTI. It is the patient's symptoms, *along with* these values, that determine the likelihood of a true UTI. This can manifest in urinary tract symptoms or more constitutional signs. In addition, generally there is evidence of inflammation in the urine, such as presence of leukocyte esterase or white blood cells at urinalysis. This constellation of signs and symptoms is important when accurately diagnosing UTI.

Pathophysiology

The factors that contribute to UTIs are not completely understood but involve bacterial and host characteristics, as well as immune status of the patient. In the pediatric population, these dynamics are constantly shifting with growth and development. A complete explanation of the pathogenesis of pediatric UTIs is outside the scope of this chapter, but we will highlight important risk factors—especially with respect to the pediatric host. In addition, it is important to distinguish infections that are isolated to the bladder, such as cystitis, and those that have renal involvement, such as pyelonephritis. Distinguishing between these infections in the pediatric patient can be difficult but can often be determined by the presence (characteristic of pyelonephritis) or absence (characteristic of cystitis) of fever. The diagnosis of pyelonephritis versus cystitis has important implications for treatment and, more importantly, for the sequela of infection, which will be further discussed later.

Bacterial Factors

Bacteria can be described as *commensal* or *virulent,* and a virulent organism is defined by its capability to cause disease. Virulent bacteria that

cause UTIs are termed *uropathogenic bacteria.* Uropathogenic organisms express traits that render them specially adapted to express virulence in the urinary tract. Commensal bacteria can also cause UTIs but do so less commonly and without the virulence factors that allow evasion of the host immune response. Because most UTIs are caused by *Escherichia coli*, its virulence factors are the most well described. Uropathogenic *E coli* have traits that allow them to subvert or hijack host defenses, permitting attachment to urogenital mucosal surfaces, interaction with tissues by setting signaling cascades and other immunologic response events, and even invasion of bladder cells (**Figure 6-1**). Uropathogenic *E coli* adaptations include fimbrial and nonfimbrial adhesins for attachment to the mucosa, metal acquisition systems suited for living in environments such as urine that are poor in iron and other necessary metals, toxins

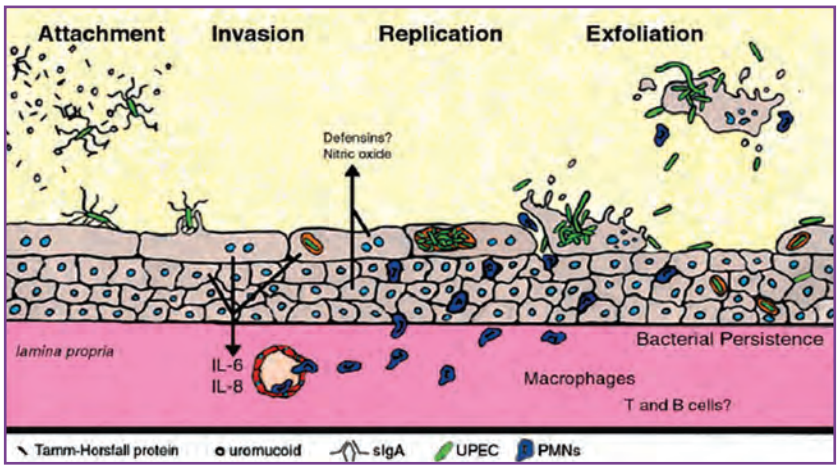


Figure 6-1. The interplay between the innate host defenses and the uropathogenic *Escherichia coli* (UPEC) within the bladder. If contact is established, FimH-receptor interactions can trigger the internalization of adherent bacteria into facet cells, in which UPEC can replicate to high levels. The release of infected bladder cells in urine may facilitate the spread of UPEC strains in the environment. To avoid clearance by exfoliation, UPEC is able to escape from dying facet cells and infect surrounding and underlying epithelial cells. These bacteria may eventually be able to enter a niche within the urothelium in which they can persist (at subclinical levels), undetected by immunosurveillance mechanisms. PMNs, polymorphonucleocytes.

Reprinted with permission from Mulvey MA, Schilling JD, Martinez JJ, Hultgren SJ. Bad bugs and beleaguered bladders: interplay between uropathogenic Escherichia coli and innate host defenses. *Proc Natl Acad Sci U S A.* 2000;97(16):8829–8835. Copyright (2000) National Academy of Sciences, USA.

for breaching barriers, nutrient release mechanisms that destroy host cells, flagella for motion, inactivators of host defenses such as enterobactin, and fimbrial phase variation mechanisms that can change antigens recognized by the host, faster than the host can adapt. Although knowledge of these factors may not seem clinically relevant to the treating physician, they represent potential therapeutic targets that are currently under investigation (**Figure 6-2**). Knowledge of bacterial traits enables development of UTI vaccine targeting strategies. In addition, current research on genetic testing in children to determine susceptibility to pyelonephritis builds on the knowledge of host responses to bacterial traits.

Host Factors

Host traits that affect UTI development in children are numerous and somewhat different than those that contribute to UTI susceptibility in adults. **Table 6-1** lists factors that can contribute to an increased incidence of pediatric UTIs.

Bladder and bowel dysfunction deserves special mention, owing to significant overlap in children with UTIs, as well as vesicoureteral reflux (VUR). Bladder and bowel dysfunction encompasses a wide spectrum of clinical presentations, including daytime and nighttime urinary

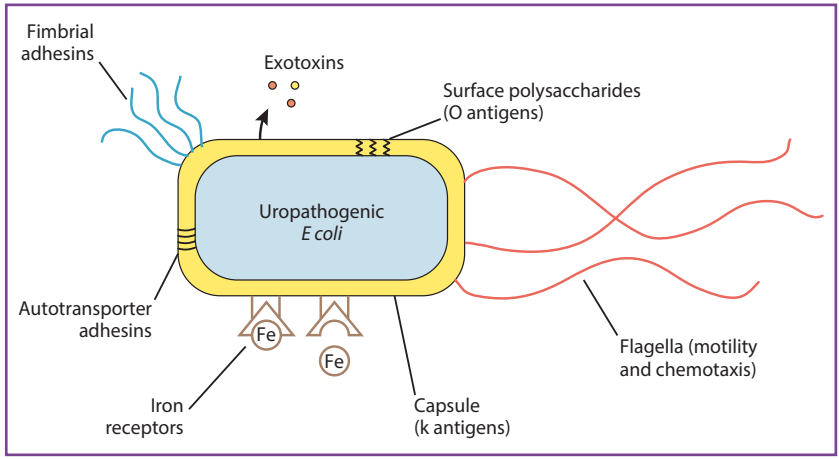


Figure 6-2. Uropathogenic *Escherichia coli* is demonstrated with fimbrial adhesions, surface polysaccharides, outer membrane iron receptors, and adhesins, which may serve as potential vaccine targets.

Table 6-1. Pediatric-Specific Host Factors That Can Contribute to Increased Risk of Urinary Tract Infection

Host Risk Factor	Specific Risk
Patient age and sex	Age <1 y: Boys > girls, incidence 2.7% boys vs 0.7% girls (only age group in which UTI prevalence is higher in boys than in girls) Prepubertal children overall: Girls > boys, incidence 3% girls vs 1% boys Postpubertal children: Girls > boys
Race	White girls > girls of other races African American boys and girls < white and Hispanic boys and girls
Genetics	No specific genes isolated Blood group antigens implicated
Circumcision status	Age <6 mo: Uncircumcised > circumcised (circumcision decreases the risk of UTI by almost 10-fold) Age >1 y: Risk reduction of circumcision unclear
Fecal and/or perineal bacterial colonization	Most UTIs are from bacteria colonizing the gut, perineum, and periurethral area ascending into the lower urinary tract. Many girls with recurrent UTIs are reinfected by the same bacterial strains persisting in the fecal microbiota.
Anatomic abnormalities	Hydronephrosis, ureteropelvic junction obstruction, ureterovesical junction obstruction, VUR, infected stones, infected nonfunctional renal segments, fistulae from the urinary tract to the intestinal or reproductive tracts
Sexual activity	Increased risk in sexually active female patients
Bladder and bowel dysfunction	Increases risk for both UTIs and VUR
Neurogenic bladder	Decreased ability to clear bacteria from the bladder, increased bladder storage pressure can increase the risk for UTI and renal damage.

Continued

Table 6-1 (*continued*)	
Host Risk Factor	**Specific Risk**
Catheter-associated UTI	Nosocomial UTIs account for 6%–18% of nosocomial infections in pediatric hospital services.
Immune status	Increased risk in the first few months after birth may be compounded by a diminished immune system.

Abbreviations: UTI, urinary tract infection; VUR, vesicoureteral reflux.

incontinence, urinary urgency, urinary frequency, constipation, and/or encopresis. Many children with these symptoms have *dysfunctional voiding*, defined by increased activity of the pelvic floor musculature during voiding, leading to incomplete bladder emptying and urinary stasis. The condition is common in children, and one study of 1,127 children showed that 29% of those sampled reported at least 1 symptom suggestive of bladder dysfunction. Of these children, 9.4% of girls and 2.8% of boys had also had at least 1 previous UTI. Treatment of bladder and bowel dysfunction has been shown to decrease recurrent UTIs and improve VUR resolution.

Long-term Outcomes

Prognosis

Along with prevention of the acute morbidity (dysuria, pain, fever) and costs of UTIs, treatment aims to prevent recurrence and long-term sequelae, including hypertension, preeclampsia, and chronic kidney disease. In general, such sequelae are only thought likely in the case of renal involvement during infection such as pyelonephritis, as compared to cystitis alone. It is difficult to predict who will develop recurrent UTIs or renal damage because of a lack of clear data on these outcomes. One multisite prospective cohort study of 500 children with a history of 1 or 2 febrile or symptomatic UTIs showed children with concomitant VUR to have the highest risk of a recurrent febrile or symptomatic UTI within 2 years (25.4%). However, a considerable risk (17.3%) in children without VUR was observed, as well. A review of 23 articles on 3,573 children demonstrated that most children with a history of febrile UTI develop

no long-term sequelae, defined as decreased renal function, hypertension, decreased growth, and pregnancy-related complications. This was especially true for children with no significant renal dysplasia at birth. It was estimated that 0.4% of children with normal renal function at the start of follow-up will experience a decline in renal function.

Renal Scarring

Scarring occurs with pyelonephritis as a result of inflammation causing local tissue damage; normal renal parenchyma is thus replaced with poorly or nonfunctioning fibrotic tissue. Scarring from pyelonephritis is known to occur more commonly at the poles of the kidney. Children with pyelonephritis and VUR are at increased risk for scar development, and risk increases with higher grades of VUR. There is an increased risk of renal scar formation with each episode of pyelonephritis, as depicted in **Figure 6-3**.

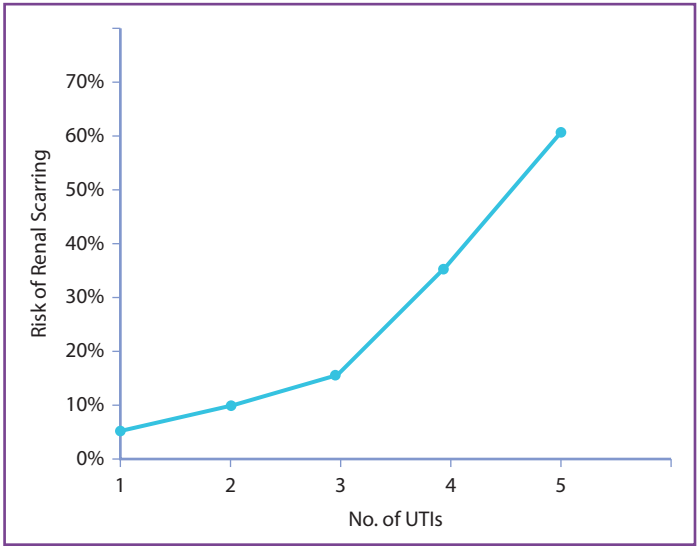


Figure 6-3. Estimated increased risk of renal scarring with each episode of pyelonephritis. UTI, urinary tract infection.

Adapted with permission from American Academy of Pediatrics Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. *Pediatrics.* 2011;128(3):595–610.

After the acute inflammatory phase, the ultimate scar involves tissue loss that is reflected radiographically by thinned renal parenchyma overlying calyces. Renal scars are best depicted on technetium 99m (^{99m}Tc) dimercaptosuccinic acid (DMSA) scans (**Figure 6-4**). Renal scars have been associated with diminished renal function and hypertension later in life. Early antibiotic treatment of pyelonephritis and prevention of subsequent episodes prevents future renal damage. Children with significant bilateral renal scars or impaired renal function warrant long-term follow-up for assessment of hypertension, renal function, and proteinuria.

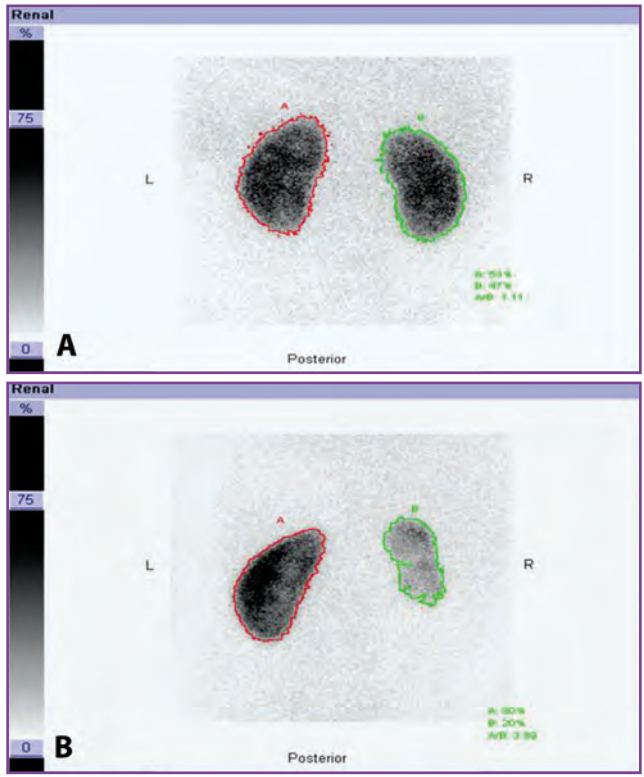


Figure 6-4. A, A technetium 99m dimercaptosuccinic acid scan is shown, with normal findings of homogeneous and symmetrical renal cortical radiotracer uptake in both kidneys, with no evidence of scarring. **B,** Bilateral renal scarring is shown, greater on the right than on the left. Focal cortical defects are associated with contraction of the renal outlines, with asymmetrical radiotracer uptake.

Adapted with permission from Zhang X, Xu H, Zhou L, et al. Accuracy of early DMSA scan for VUR in young children with febrile UTI. *Pediatrics.* 2014;133(1):e30–e38.

Diagnosis and Evaluation

Classification of Urinary Tract Infections

Diagnosis of a UTI is not always straightforward, especially when guidelines differ as to what establishes a diagnosis. At its most basic, a UTI is the invasion of the urinary tract by an organism that leads to pathologic changes, due either to the organism itself or to the host response. Demonstration of a UTI requires proof of the organism in the urinary tract (usually provided through urine culture) and confirmation that the organism is pathogenic (usually validated by symptoms and/or evidence of immune response in urine or blood tests). Diagnosis of UTI is discussed in the Laboratory Studies section. UTIs can be classified in myriad ways, but it is clinically useful to think about them as upper tract–febrile versus lower tract–afebrile, since the management approaches differ considerably. A child is generally considered to have an upper tract infection (pyelonephritis) if the presentation includes high fevers, vomiting, flank pain, or lethargy. A child is usually considered to have a lower tract infection (cystitis) if he or she is afebrile with predominantly urinary symptoms, such as dysuria, urgency, or frequency. Making this distinction on the basis of symptoms alone may yield a correct diagnosis, but the standard of reference for diagnosis of pyelonephritis is a DMSA scan. Less common than pyelonephritis is a more severe acute bacterial nephritis that consists of inflammation from pyelonephritis spreading throughout the kidney, with focal areas of necrosis. Renal abscesses may have a presentation similar to pyelonephritis but with a negative urine culture result in up to 20% of patients (**Figure 6-5**). In general, UTI is defined by the presence of urinary symptoms or constitutional symptoms, along with urinalysis findings consistent with inflammation (eg, findings positive for leukocyte esterase and/or white blood cells at microscopy) or bacteria on gram stain and presence of a single bacterial pathogen in the urine, as confirmed with a urine culture. As stated earlier, the number of CFU per milliliter depends on the method of urine collection (>50,000 CFU for a catheter sample or suprapubic aspiration sample vs >100,000 CFU for a clean-catch sample).

Asymptomatic bacteriuria (ASB) is defined as the growth on 2 consecutive urine cultures of more than 100,000 CFU/mL of the same uropathogen in a patient with no symptoms of infection. It is unclear why

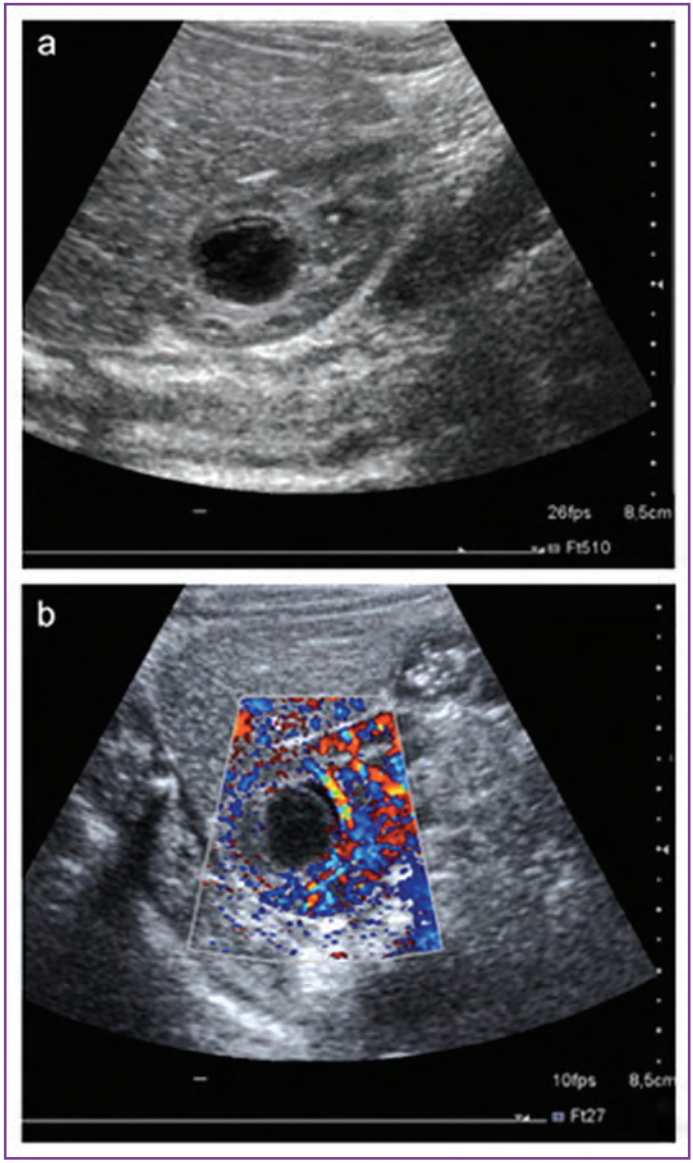


Figure 6-5. Pediatric renal ultrasonographic images depict a renal abscess. **A,** A hypoechoic region within the renal parenchyma is surrounded by a thin, hyperechoic rim. **B,** Power Doppler image shows no vascular signal within the central area but a well-vascularized periphery.

Adapted with permission from Comploj E, Cassar W, Farina A, et al. Conservative management of paediatric renal abscess. *J Pediatr Urol.* 2013;9(6 Pt B):1214–1217.

patients with ASB develop this urinary tract colonization rather than overt infection. With an estimated prevalence of 1% to 2% in school-aged girls and 0% to 0.1% in school-aged boys, it is a distinct clinical entity from a UTI, in that neither screening for ASB nor antibiotic treatment are warranted. Children with ASB but without any genitourinary anomalies do not appear to be at increased risk for recurrent symptomatic infections, renal damage, or impaired renal growth without treatment.

Although this chapter focuses on bacterial UTIs, viral cystitis and funguria do occur in the pediatric population, as well. Viral cystitis, often caused by adenovirus and sometimes BK polyomavirus, can cause acute and sometimes severe hemorrhagic cystitis. Viral cystitis is commonly seen in immunosuppressed individuals, often after bone marrow transplantation. Fungal UTIs are also associated with immunocompromised individuals, as well as those who have recently received antibiotics and have an intravenous and umbilical artery catheterization or indwelling urinary catheter. *Candida* species are the most common causes of fungal UTI, and asymptomatic funguria is common with a catheter in place. When repeated urine cultures show more than 10,000 to 15,000 CFU/mL, treatment is generally recommended. Fluconazole has been successfully used for funguria in children but is contraindicated in infants younger than 6 months.

History and Physical Examination

Box 6-1 presents an overview of clinical findings to be considered in the pediatric patient. Clinical presentation and management strategies vary on the basis of patient age.

Approach to Infants and Children Younger Than 24 Months

UTIs account for 7% of diagnoses in the febrile infant. Symptoms are often vague and nonspecific, leading to delayed diagnosis and treatment. Fever is usually the primary symptom leading to diagnosis, but symptoms can also include irritability, poor feeding, jaundice, failure to thrive, vomiting, diarrhea, abdominal distention, and foul-smelling urine. In children younger than 24 months who have a fever, a temperature higher than 40°C (104°F), history of previous UTI, suprapubic tenderness, and uncircumcised penis are the most useful signs and

Box 6-1. History and Physical Examination Elements to Consider for Suspected Urinary Tract Infection

History

Constitutional symptoms
- Fever
- Irritability
- Failure to thrive
- Poor oral intake
- Fatigue, malaise

Vomiting

Diarrhea

Foul-smelling urine

Suprapubic and/or flank pain

Voiding symptoms
- Dysuria
- Worse daytime, nighttime incontinence
- Gross hematuria
- Worse urinary frequency, urgency
- Urinary dribbling
- Weak stream

Constipation, encopresis (could indicate bladder and bowel dysfunction)

Irritants
- Detergents, fragrances, soaps, fabrics that may cause local irritation

Diet and fluid intake
- Dehydration, dietary factors that can increase urinary symptoms (coffee, citrus)

Previous history
- Previous UTI, recurrent UTI
- Genitourinary anatomic abnormalities (VUR)
- Abnormal prenatal and/or postnatal US findings

Surgical history

Previous genitourinary or gastrointestinal surgery

Family history
- Family history of UTI, VUR, other genitourinary abnormalities

Sexual history
- Sexual abuse
- Timing of UTIs in a sexually active adolescent

Physical Examination

General appearance
- Jaundice
- Lethargy
- Toxicity

Vital signs
- Temperature
- Tachycardia
- Blood pressure (Hypertension could indicate chronic renal insufficiency.)

Growth parameters
- Delayed growth (could indicate chronic renal insufficiency)

Abdomen
- Suprapubic tenderness
- Costovertebral angle tenderness (indicates pyelonephritis)
- Abdominal distention/mass (could indicate constipation or full bladder)

Box 6-1 (*continued*)

Physical Examination (*continued*)

- Flank mass (could indicate hydronephrosis)

Genital (general)

- Trauma
- Local irritation
- Urethral discharge
- Foreign body
- Anatomic abnormalities

Genitals (male)

- Testicular swelling or tenderness (could indicate epididymo-orchitis)
- Urethral meatal stenosis
- Phimosis
- Urethral ballooning (could indicate urethral diverticulum)

Genital (female)

- Vaginal discharge
- Ectopic ureter
- Labial adhesions
- Urethral mass

Back (Rule out spina bifida occulta.)

- Asymmetrical gluteal cleft
- Sacral dimple
- Gluteal fat pad
- Hypertrichosis

Neurological (Rule out neurogenic bladder.)

Abbreviations: US, ultrasonography; UTI, urinary tract infection; VUR, vesicoureteral reflux.

symptoms for prediction of UTI. Other symptoms, such as poor feeding, vomiting, and irritability, are not sensitive or specific but are commonly associated with UTI in this age group. Because of the poor specificity of symptoms and the difficulty with obtaining a urine sample in this age group, the American Academy of Pediatrics (AAP) 2011 guidelines contain an action statement to help providers determine which febrile infants and children between the ages of 2 and 24 months should be tested for UTI. The recommendation states that if the infant with fever of unknown origin is not so ill as to require immediate antibiotic therapy, the likelihood of UTI should be considered. If the likelihood of UTI is low (<1%), urine testing may be deferred. It is known that the probability of a UTI in an uncircumcised febrile boy exceeds 1%, without any additional risk factors. In girls and circumcised boys, the risk has been shown to be up to 1% by allowing for a single risk factor in girls and up to 2 risk factors in circumcised boys, but the risk is 2% when more risk factors are present. Thus, a urine sample should be obtained in most febrile patients in this age group.

Although the risk for UTI is less when another potential source of fever has been identified, the diagnosis cannot be completely ruled out. One study of 2,411 febrile infants and children showed a UTI prevalence of 5.9% in children without an identified source, compared with 2.7% in children with another potential source identified. The diagnosing clinicians in this study incorrectly attributed another source of fever to 64% of children with a UTI. This example highlights the need to consider the possibility of a UTI in any febrile infant or child, *even if another source has been identified.*

Physical examination should be thorough and include abdominal, genital, back, and focused neurological examinations, despite the frequency of nonspecific findings.

Approach to Children Older Than 24 Months

UTIs account for 7.8% of fevers in children older than 24 months. Additionally, as children begin to verbalize their discomforts, symptoms more classically associated with adult UTIs may become more apparent. Dysuria, new or worsening incontinence, changes in voiding habits, new or worsening enuresis, and flank and abdominal pain can all be reported and increase the likelihood of UTI diagnosis. However, it must be kept in mind that these symptoms are nonspecific for UTI and are also often seen in children with bowel and bladder dysfunction and in girls with vulvovaginitis.

In both infants and older children, other risk factors for UTI should be sought, including previous personal and family histories of UTI, VUR, and other genitourinary abnormalities. In adolescents, a sexual history should be obtained. In older children, physical examination may be notable for suprapubic, abdominal, or flank tenderness—the latter being suggestive of pyelonephritis.

In the Diagnosis and Treatment of Urinary Tract Infection in Young Children in Primary Care (DUTY) study, clinical predictors of UTI were assessed in 2,740 children younger than 5 years who presented to the primary care setting with at least 1 symptom or sign of UTI. Researchers created a model to help clinicians decide if a urine sample should be obtained in a child presenting to the primary care setting. The model was found to be more accurate than clinician suspicion for UTI alone. Predictors of UTI included previous UTI, pain and/or crying with the passage of urine, foul-smelling urine, absence of severe cough, increased

clinician impression of severe global illness, abdominal tenderness at examination, and normal ear examination findings. Notably, there was no increased probability for UTI with fever, fever of unknown origin without another identifiable source of infection, vomiting, irritability, lethargy, poor feeding, or duration of prior illness.

Laboratory Studies

Modes of Urine Collection

Urine collection for demonstration of organisms present in the urinary tract is mandatory to establish a diagnosis of UTI. Additionally, current AAP guidelines mandate evidence of infection at urinalysis, such as pyuria (presence of white blood cells [WBCs] in the urine) and/or bacteriuria, to help distinguish true infection from ASB and contamination. The risk of obtaining a contaminated urine specimen increases with decreased invasiveness of urine collection. Consequences of UTI overdiagnosis include unnecessary antibiotic treatment with inherent costs and side-effects, increased risk of bacterial antibiotic resistance, and potential unnecessary, expensive, and invasive imaging for further evaluation. A missed diagnosis could lead to increased severity of illness, hospitalization, or renal scarring. Thus, accurate diagnosis prior to initiation of antibiotics is critical.

The least invasive method of urine collection is via diaper pad or collection bag affixed to the perineum. The false-positive rate is high with this method through perineal and rectal flora contamination, as well as contamination with WBCs from outside of the urinary tract. False-positive findings from bag sampling have been estimated at an unacceptably high rate of 85% to 99%. Urine collection via this method is only helpful when not indicative of a UTI. However, it can be considered as screening before moving to more invasive methods.

Although not an option in children before toilet training, a clean-catch urine sample is also relatively noninvasive. It is more reliable in older girls and circumcised boys but still has a higher chance of contamination than suprapubic aspiration or catheterization.

The AAP recommends urethral catheterization or suprapubic aspiration for urine collection in non–toilet-trained children younger than 24 months. Disadvantages include invasiveness and potential for trauma or introduction of infection. Suprapubic aspiration via

a 22-gauge needle is considered the standard of reference for sterile urine collection, but its use is often not practical, given the need for performance by a skilled practitioner and possible ultrasonographic (US) guidance. Although considered unacceptably invasive by some, it may be necessary in boys with tight phimosis or girls with dense labial adhesions. When compared with suprapubic aspiration, a clean-catch specimen for culture has a sensitivity of 75% to 100% and a specificity of 57% to 100%. When compared to suprapubic aspirate, a catheterized urine specimen has a sensitivity of 95% and specificity of 99%.

Catheter insertion should be performed in a sterile fashion. The use of intraurethral and/or topical lidocaine 2 to 10 minutes prior to catheterization has been shown to reduce discomfort and distress from catheterization. Urethral catheterization in girls often requires a 2-person technique, with one person exposing the urethral meatus and the other person inserting the catheter. The normally recessed urethral opening and surrounding anatomic landmarks can be identified most easily by placing gentle traction on each of the labia majora, outward and slightly lateral. The tendency with a 1-handed technique is to pull the labia too far laterally, which can cause significant pain and trauma, making subsequent catheterization more difficult. Once the catheter is inserted, the first few drops of urine obtained should not be collected for specimen, as they are the most likely to be contaminated.

Urinalysis

Although a urine culture is the standard of reference for UTI diagnosis, urine dipstick and microscopic urinalysis can provide more rapid screening for UTI. In general, urinalysis has also been considered a complementary form of diagnosis, but in the AAP guidelines for diagnosing UTI in patients 2 to 24 months of age, urinalysis is considered a necessary diagnostic tool. Urinalysis testing should be performed on urine less than 1 hour after voiding if kept at room temperature or less than 4 hours if refrigerated. Summary estimates for sensitivity and specificity for methods of urinalysis alone and in combination are shown in **Table 6-2**.

Urine Dipstick Testing

The most useful parameters for urine dipstick testing in UTI are leukocyte esterase and nitrite. Leukocyte esterase is released when WBCs are

Table 6-2. Summary Estimates for Sensitivity and Specificity of Components of Urinalysis, Alone and in Combination

Test	Sensitivity, % (95% CI)	Specificity, % (95% CI)
Leukocyte esterase (dipstick)	79 (73–84)	87 (80–92)
Nitrite (dipstick)	49 (41–47)	98 (96–99)
Positive for *either* leukocyte esterase *or* nitrite (dipstick)	88 (82–91)	79 (69–87)
Positive for *both* leukocyte esterase *and* nitrite (dipstick)	45 (30–61)	98 (96–99)
Unstained bacteria (urine microscopy)	88 (75–94)	92 (83–96)
Gram stain (urine microscopy)	91 (80–96)	96 (92–98)
White blood cell count (urine microscopy)	74 (67–80)	86 (82–90)

Abbreviation: CI, confidence interval.
Adapted with permission from Williams GJ, Macaskill P, Chan SF, Turner RM, Hodson E, Craig JC. Absolute and relative accuracy of rapid urine tests for urinary tract infection in children: a meta-analysis. *Lancet Infect Dis.* 2010;10(4):240–250.

broken down in the urine, serving as a marker for pyuria. False-positive findings can be caused by other causes of inflammation in the urine, but AAP guidelines suggest the absence of leukocyte esterase in the urine helps distinguish ASB from true UTI, in that the absence of pyuria in a child with a true UTI is rare. The cutoff for a positive leukocyte esterase test result (trace, small, or moderate) has not been definitively established. A recent retrospective cross-sectional study of 2,700 children showed an 88% and 79% sensitivity and 96% and 97.5% specificity in dilute and concentrated urines, respectively, by using a cutoff of low leukocyte esterase values.

Urinary nitrite is reduced from dietary nitrates in the urine by gram-negative enteric bacteria. This conversion takes several hours to occur, so a urine collection first thing in the morning is the most sensitive with this test, and frequent urination or dilute urine can generate false-negative results. Additionally, infection with gram-positive organisms will result in a false-negative finding. Sensitivity is poor, but specificity

is excellent, meaning that a positive nitrite test result is likely to reflect true UTI.

Urine Microscopy

Traditionally, pyuria is assessed with microscopy from a centrifuged urine specimen by using a threshold of 5 WBCs per high-power field (HPF). However, a threshold of 10 WBCs/HPF has been considered a more accurate predictor of UTI in children younger than 2 years by the National Institute for Health and Care Excellence, the Italian Society of Pediatric Nephrology, and the Royal Children's Hospital Melbourne guidelines. Urine microscopy for WBCs alone does not appear to be more accurate than dipstick leukocyte esterase for determination of UTI. Glissmeyer and colleagues retrospectively examined the catheterized urine testing of 6,394 febrile neonates younger than 90 days, 770 (12%) of whom had UTIs at culture. The positive predictive value of the urine dipstick alone was significantly better than that of urine microscopy, as well as the dipstick combined with microscopy, but the negative predictive value of urine dipstick alone was inferior when compared to the combined method. Researchers concluded that 8 febrile infants would have a false-positive combined urinalysis result for every 1 infant with a UTI missed with dipstick screening. Additive value of urine microscopy to the urine dipstick method remains to be demonstrated. The disadvantages of microscopy include increased expense, need for laboratory use, and a longer time needed to obtain results.

The most reliable and rapid test for the diagnosis of UTI consists of the microscopic identification of bacteria on both unstained and gram-stained uncentrifuged fresh urine specimens. Both sensitivity and specificity for microscopic bacteria are improved with Gram staining.

Urine Culture

A positive urine culture finding is essential for the diagnosis of a UTI, but there is debate on what constitutes a positive urine culture result. Historically, a UTI has been characterized by at least 10^5 CFU/mL of a single uropathogen. However, this value was based on early-morning voided samples in adult women, which may not be applicable in children. The 2011 AAP guidelines suggest that the threshold be reduced to 50,000 CFU/mL with the presence of pyuria and/or bacteriuria at urinalysis from a catheterized or suprapubic aspirate sample in children

aged 2 to 24 months. The European Association of Urology suggests that 10^4 CFU/mL be used with a clean-catch specimen if associated with symptoms but 10^5 CFU/mL if there are no symptoms. Still other guidelines further consider the urine collection method and risk of contamination. Contamination must be considered in cases with low colony counts; cultures with heavy, mixed growth of bacteria; and cultures that are growing nonpathogenic organisms like *Lactobacillus,* coagulase-negative staphylococci, *Corynebacterium*, α-hemolytic streptococci, and *Candida* species. However, even when contamination is suspected, a concurrent true infection must be considered.

Serum Tests

Serum markers, including WBC count, serum creatinine level, C-reactive protein level, erythrocyte sedimentation rate, and procalcitonin level, have been evaluated as measures to assess UTI severity or differentiate between cystitis and pyelonephritis. However, none have been shown to be effective in altering clinical management. These measures can be used to evaluate clinical progress and response to treatment.

Radiologic Imaging

Not unlike other aspects of pediatric UTI, there is debate regarding the appropriate imaging method to use after the first febrile UTI in a child. Historically, a standard workup included renal and bladder US and voiding cystourethrography (VCUG). VUR is the most common genitourinary anomaly seen, identified in up to 40% of children with a febrile UTI. However, because of a lack of evidence supporting the routine use of imaging in decreasing long-term sequelae of pyelonephritis, such as renal scarring and renal insufficiency, recommendations vary widely (**Table 6-3**). Unfortunately, the goal of identifying and testing only those children that will ultimately benefit from that testing has not yet been achieved.

Ultrasonography

Renal and bladder US (RBUS) can show the size, shape, and presence of both kidneys, as well as allow screening for undiagnosed congenital abnormalities, urinary tract obstruction, hydronephrosis, stones, pyonephrosis, and fluid collections, such as renal or perirenal abscesses. RBUS is estimated to yield abnormal findings in about 15% of infants

Table 6-3. Summary of 5 Guidelines for Imaging After First Febrile Urinary Tract Infection in an Infant

Guidelines	Renal US	VCUG	Late DMSA Scan
RCH	Yes, but not for a first UTI unless the patient is a male neonate <3 mo of age, the patient is seriously unwell, or the patient has renal impairment	If boy <6 mo and/or positive US findings	No
NICE			
<6 mo	Yes	If positive US findings and/or atypical UTI[a]	If atypical UTI[a]
≥6 mo	If atypical UTI	If child with risk factors[b]	If atypical UTI[a]
TDA	No	If positive, acute DMSA finding	If positive, acute DMSA finding
AAP	Yes	If positive US findings	No
ISPN	Yes	If positive US findings or if children have risk factors[c]	If positive US and/or VUR finding

Abbreviations: AAP, American Academy of Pediatrics; DMSA, technetium 99m-dimercaptosuccinic acid; ISPN, Italian Society of Pediatric Nephrology; NICE, National Institute for Health and Care Excellence; RCH, Royal Children's Hospital Melbourne; TDA, top-down approach; US, ultrasonography; UTI, urinary tract infection; VCUG, voiding cystourethrography; VUR, vesicoureteral reflux.

[a] Seriously ill, poor urine flow, abdominal or bladder mass, increased creatinine level, septicemia, failure to respond to correct antibiotic treatment within 48 hours, or infection with non–*Escherichia coli* organisms.

[b] Dilatation at US, poor urine flow, non–*E coli* infection, or family history of VUR.

[c] Abnormal prenatal US findings of the urinary tract, family history of VUR, septicemia, renal failure, age younger than 6 months in a male infant, likely noncompliance of the family, abnormal bladder emptying, no clinical response to correct antibiotic treatment within 72 hours, or non–*E coli* infection.

Adapted with permission from La Scola C, De Mutiis C, Hewitt IK, et al. Different guidelines for imaging after first UTI in febrile infants: yield, cost, and radiation. *Pediatrics.* 2013;131(3):e665–e671.

and young children after an initial febrile UTI. It is estimated that 1% to 2% of these children will have an abnormality that requires additional evaluation or treatment. If a child is not responding appropriately to treatment for UTI within 48 hours or is unusually ill, US should be performed during the acute episode, as urgent intervention may be warranted. On the other hand, acute pyelonephritis can sometimes cause misleading dilatation of the collecting system and changes in the renal parenchyma, leading to false-positive results, so if a child responds appropriately to treatment, RBUS can be delayed. Other limitations of routine US include a low sensitivity for the detection of VUR, as seen in **Figure 6-6**, and low sensitivity for renal scarring or injury compared to nuclear scintigraphy.

Additionally, the accuracy of RBUS is operator dependent. Despite its drawbacks, RBUS has generally been accepted as a common initial imaging study, as it is noninvasive, free from radiation exposure, and widely available. Even if a child has had an abnormal antenatal US finding, repeat US should be strongly considered, given the variability in quality and timing with prenatal US. Current AAP guidelines recommend performing RBUS in all children younger than 2 years who have a febrile UTI. Additional indications for RBUS include recurrent febrile or afebrile UTIs, failure to respond to culture-driven antibiotic therapy, non–*E coli* UTIs, hypertension, or a family history of renal or urological disease.

Voiding Cystourethrography

VCUG can be performed by instillation of iodinated contrast medium into the bladder and performing subsequent fluoroscopy or instillation of a nuclear imaging agent, such as ^{99m}Tc pertechnetate. Contrast-enhanced VCUG is much more common than radionuclide cystography and is considered the reference-standard imaging technique for detection and grading of VUR. Additionally, VCUG can be used to evaluate bladder size and shape, presence of trabeculations and diverticula, and functional or anatomic urethral abnormalities that may indicate bladder outlet obstruction or neurogenic bladder. VCUG can also show constipation or a spinal defect consistent with spina bifida occulta.

In the evaluation of a child with a UTI, VCUG can be performed as soon as the child is asymptomatic and demonstrating his or her normal voiding pattern. Disadvantages of VCUG include invasive nature and

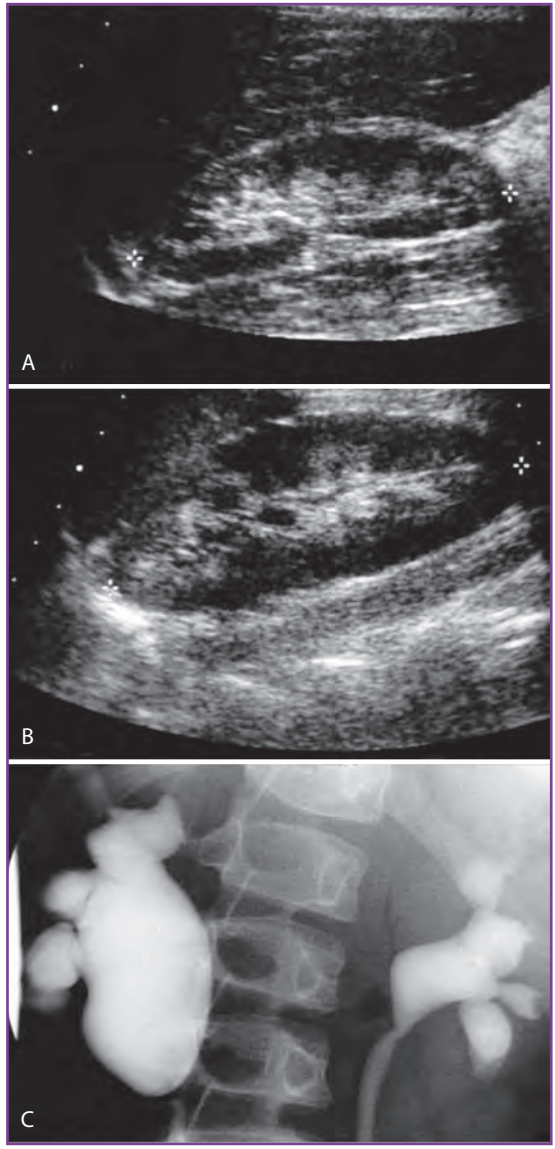


Figure 6-6. A, B, Normal ultrasonographic findings of the right and left kidneys, despite the presence of high-grade vesicoureteral reflux, as seen with (**C**) voiding cystourethrography.

Reprinted with permission from Nguyen HT. Obstructive uropathy and vesicoureteral reflux. In: McInerny TK, Adam HM, Campbell DE, DeWitt TG, Foy JM, Kamat DM, eds. *American Academy of Pediatrics Textbook of Pediatric Care.* 2nd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2017:2412.

radiation exposure. The radiation reported from VCUG ranges from 0.5 to 3.2 mSv, with 1 mSv noted as the commonly accepted value.

The most recent AAP guidelines do not recommend routinely performing VCUG after the first febrile UTI in a child younger than 24 months, unless RBUS findings are outside reference range. VCUG is recommended if there is a recurrence of febrile UTI. The AAP Section on Urology issued a rebuttal, stating that the AAP guidelines were based on premature conclusions and represented misinterpretation of data. The section disagreed that routine VCUG is unwarranted after the first febrile UTI. It recommended that VCUG remain an accepted initial diagnostic option, as some children with VUR do benefit from early detection and treatment to prevent recurrent infection and renal damage. Additional concern was expressed that it may be difficult to differentiate between the first febrile UTI and recurrent episodes. VCUG should also be considered in older children with recurrent febrile UTIs, especially if there is a known family history of VUR.

Technetium 99m Dimercaptosuccinic Acid Scanning

Cortical renal scanning with DMSA, combined with single photon emission computed tomography, is considered the standard of reference for the identification of parenchymal renal lesions. An alternative approach to imaging in the child with a febrile UTI is termed the "top-down approach." It consists of obtaining a DMSA scan at the time of the first febrile UTI and performing VCUG only in those with an abnormal DMSA scan finding. This approach relies on the findings that renal scarring only occurs in the presence of renal inflammation. Confirming true renal involvement with DMSA at the time of presumed pyelonephritis truly identifies patients at risk for renal scarring. By deferring VCUG, only about 15%–30% of VUR may be missed, but this approach is less specific than other imaging approaches. Nuclear scintigraphy is also costly, and timing affects its sensitivity for determination of renal involvement with an acute UTI. If the scan is performed 3 weeks or more after pyelonephritis is diagnosed, the findings might be within reference range, as the photopenic defect can resolve. The radiation dose for DMSA scintigraphy has been estimated at about 1 mSv.

DMSA scans are useful for detecting chronic renal scars and estimating differential renal function. Renal scars appear as regions of decreased uptake in the cortex but may be indistinguishable from areas of

congenital renal dysplasia frequently associated with VUR. The degree of renal scarring has been shown to be more significant in children with higher grades of VUR. Assessment of irreversible renal scarring should not be performed earlier than 6 months after an acute episode of pyelonephritis; some suggest waiting up to 1 to 2 years for resolution of reversible defects. Other nuclear agents, such as ^{99m}Tc mercaptoacetyltriglycine, are sometimes used with less detailed imaging of the renal cortex but better visualization of the collecting system, which is helpful in the assessment of urinary obstruction.

Computed Tomography and Magnetic Resonance Imaging

Although both computed tomography and magnetic resonance imaging provide excellent anatomic detail of the urinary tract, their practical use in the diagnosis and management of UTI in children is limited, given the high amount of radiation exposure in the former and the expense and potential need for sedation in the latter.

Differential Diagnoses

For differential diagnoses of UTIs, see **Box 6-2**.

Treatment Options and Outcomes

Antibiotic Treatment

The goals of antibiotic treatment for UTI include not only amelioration of symptoms and eradication of a uropathogen but also the prevention of renal scarring. Early antibiotic treatment of a febrile UTI is critical in limiting renal involvement and renal scarring. The rate of scar formation seen on DMSA scans in one study increased from 11% to 76.5% when antibiotics were initiated 6 days from onset of symptoms, instead of 2 days. Antibiotics often need to be started empirically, especially given nonspecific symptoms in young children and definitive diagnosis with urine culture usually taking 2 to 3 days to return. Empirical antibiotic treatment based on symptoms, signs at physical examination, urinalysis, and serum testing should be confirmed and adjusted on the basis of subsequent urine culture results. In one review of more than 40,000 episodes of care in which children were treated for UTI, urinalysis was only performed in 75% of cases, and urine culture was obtained

Box 6-2. Differential Diagnoses of Pediatric Urinary Tract Infection

Infants and Children <24 Months of Age

When fever is the primary presenting symptom, rule out
- Acute otitis media
- Gastroenteritis
- Upper respiratory tract infection

If fever source is unknown, consider
- Viral infection
- Occult bacteremia

Children >24 Months of Age (Verbal Children)

If there are urinary symptoms, consider
- Urinary calculi
- Urethritis
- Sexually transmitted infection
- Sexual abuse
- Bowel and bladder dysfunction
- Foreign body
- Vulvovaginitis
- Epididymo-orchitis
- Diabetes
- Dehydration (concentrated urine)
- Appendicitis
- Fungal or viral cystitis
- Hypercalciuria

a little more than half the time. This practice can lead to overtreatment of those who do not truly have a UTI or undertreatment and therapeutic delay in those who have a UTI but require a different antibiotic because of bacterial resistance. Additionally, indiscriminate use of broad-spectrum antibiotics leads to bacterial resistance and increased side effects.

Inpatient Versus Outpatient Management

A very small proportion of children with acute UTIs will require inpatient admission, but the decision should be based on age and clinical status. Indications for hospitalization include neonates younger than 1 month (or infants younger than 2–6 months, according to some),

toxic presentation, dehydration, intolerance of oral intake, or questionable compliance with antibiotics. A febrile UTI in newborns and young infants proceeds to urosepsis and resultant electrolyte abnormalities more frequently than in older children. Thus, newborns and young infants require hospitalization, a full septic evaluation, and parenteral antibiotics until the clinical condition has improved and culture results have returned. Nontoxic neonates and infants older than 2 months and children with suspected pyelonephritis can be treated as outpatients, as long as antibiotic compliance and tolerance are not issues. Several randomized studies have shown no significant differences between the oral and intravenous routes in terms of time to clinical improvement or progression to renal scars.

Antibiotic Duration

With acute afebrile cystitis, an antibiotic course of 2 to 4 days has been shown to be noninferior to a 7- to 14-day course and leads to decreased UTI recurrence when compared with a single dose or 1-day antibiotic course. For a febrile UTI in children, a 7- to 14-day course has proven to be superior to a shorter course, although data on the comparison of 7, 10, and 14 days are inconclusive. The total course of therapy, whether oral or parenteral, should range from 7 to 14 days for a febrile UTI and in UTIs complicated by anatomic abnormalities or the presence of foreign bodies. A renal abscess can often be treated with antibiotics alone, but failure to respond could necessitate drainage.

Antibiotic Selection

When choosing an empirical antibiotic for treatment of UTI, presence of cystitis or pyelonephritis, bacterial antibiotic resistance patterns, patient age and sex, allergies, previous antibiotic exposure, previous culture results, and patient comorbidities must be considered. *E coli* remains the most common uropathogen in pediatric UTIs, causing more than 80% of infections. Keeping in mind individual patient characteristics, nitrofurantoin or a first-generation cephalosporin is often an appropriate narrow-spectrum antibiotic choice. However, nitrofurantoin has poor tissue penetration and should never be used for a febrile UTI or for suspected pyelonephritis. Trimethoprim (TMP)-sulfamethoxazole (SMX) and amoxicillin are used in about 50% of outpatient visits,

but these may be a poor empirical choice for UTI, given high *E coli* resistance rates. Empirical treatment of a UTI should also be based on local and regional antibiograms that are revised and published annually, since uropathogen prevalence and antibiotic resistance change over time.

In addition to *E coli*, other common gram-negative bacterial uropathogens include *Klebsiella*, *Proteus*, *Enterobacter*, and *Citrobacter*. Gram-positive organisms include *Staphylococcus saprophyticus*, *Enterococcus*, and, rarely, *Staphylococcus aureus*. Neonates and young infants should be covered for *Enterococcus* species empirically, as the incidence of these infections is higher in this age group. *Enterococcus* species are usually sensitive to ampicillin and first-generation cephalosporins. A combination of ampicillin and a third-generation cephalosporin or aminoglycoside is considered a safe empirical choice for infants receiving parenteral therapy. Aminoglycosides should be considered for patients at risk for *Pseudomonas* UTIs, like those with recent antibiotic exposure, recent hospitalization, or urinary tract abnormalities. Parenteral antibiotics may be converted to an oral option on the basis of culture results and the child's clinical picture, including defervescence.

Narrow-spectrum antibiotics should be used when possible, but empirical broad-spectrum therapy should be used for those at risk for resistant UTIs, such as those with a history of previous UTI, recent antibiotic exposure, recent hospitalization, or genitourinary abnormality.

Nitrofurantoin has been associated with an increased risk of hemolytic anemia in neonates younger than 3 months, so it should not be used in this population. TMP-SMX is contraindicated in preterm neonates and term newborns younger than 6 weeks. Although fluoroquinolones are effective against uropathogens, their use in children should be very limited, since widespread resistance to them has ensued from common prescription, and their safety in children is under investigation. **Table 6-4** shows common oral and parenteral antibiotic dosing, side effects, and inpatient and outpatient resistance patterns to common uropathogens on the basis of national data from The Surveillance Network. Resistance rates will vary on the basis of region.

Figure 6-7 depicts a general management algorithm for the evaluation and management of a febrile UTI.

Continued on page 149

Table 6-4. Common Therapeutic Antibiotic Dosing, Side Effects, and Inpatient and Outpatient Uropathogen Resistance Rates

Antibiotic	Oral or IV	Dose	Side Effects and Contraindications	Inpatient and Outpatient Uropathogen Percentage Antibiotic Resistance (%)					
				Escherichia coli	*Entero-bacter*	*Entero-coccus*	*Klebsiella*	*Proteus mirabilis*	*Pseudomonas aeruginosa*
Narrow-spectrum Antibiotics									
TMP-SMX	Oral	8–10 mg/k/d TMP in 2 doses	Diarrhea, nausea, vomiting, photo-sensitivity, rash; contraindicated in neonates <6 wk and in renal failure	30/24	13/18	X/X	17/15	13/11	95/94
Ampicillin	IV	50 mg/kg/d divided into doses given every 6-8 h; >40 kg, 500 mg IV given every 6 h	Diarrhea, rash	55/45	80/78	13/3	82/81	11/12	X/X
Nitrofurantoin	Oral	5–7 mg/kg/d in 4 doses	Nausea, vomiting, bad taste; contrain-dicated in neo-nates <3 mo, renal insufficiency, G6PD deficiency	<1/<1	21/23	5/1	13/17	88/94	0/0
Cefazolin	IV	25–50 mg/kg/d in 3–4 doses	Diarrhea, rash	8/4	93/91	X/X	13/7	4/4	X/X

Table 6-4 (*continued*)

Antibiotic	Oral or IV	Dose	Side Effects and Contraindications	Inpatient and Outpatient Uropathogen Percentage Antibiotic Resistance (%)					
				Escherichia coli	*Entero-bacter*	*Entero-coccus*	*Klebsiella*	*Proteus mirabilis*	*Pseudomonas aeruginosa*
Narrow-spectrum Antibiotics (*continued*)									
Cephalexin	Oral	50–100 mg/kg/d in equally divided doses	Diarrhea, rash						
Gentamicin	IV	7.5 mg/kg/d divided into doses given every 8 h or single daily dosing	Nephrotoxicity	/4	/2	/X	/3	/5	/10
Vancomycin	IV	40 mg/kg/d divided into doses given every 6 h	Abdominal pain, diarrhea, nausea, vomiting, hypokalemia, nephrotoxicity	X/X	X/X	6/<1	X/X	X/X	X/X
Broad-spectrum Antibiotics									
Amoxicillin/clavulanic acid	Oral	<40 kg, 20–40 mg/kg/d in 3 doses; >40 kg, 500–875 mg given every 12 h	Diarrhea, nausea, vomiting, rash	6/5	X/91	X/X	4/4	0/1	X/X

Continued

Table 6-4 (*continued*)

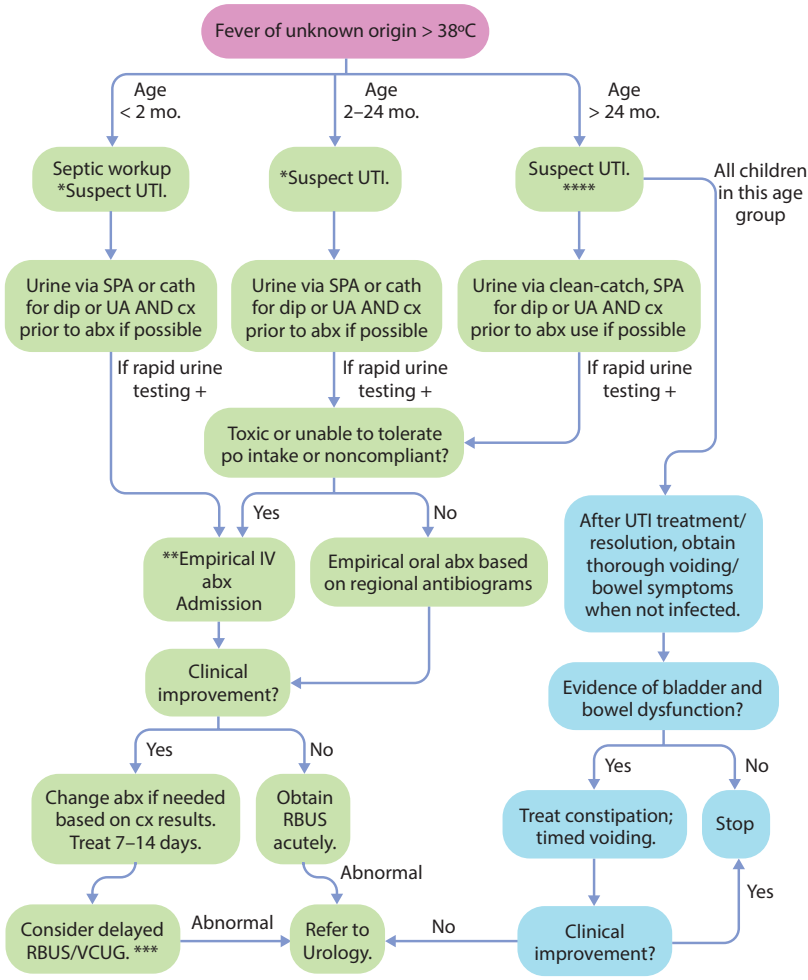
Antibiotic	Oral or IV	Dose	Side Effects and Contraindications	Inpatient and Outpatient Uropathogen Percentage Antibiotic Resistance (%)					
				Escherichia coli	*Entero-bacter*	*Entero-coccus*	*Klebsiella*	*Proteus mirabilis*	*Pseudomonas aeruginosa*
Broad-spectrum Antibiotics (*continued*)									
Cefuroxime	IV	50–100 mg/kg/d, divided into doses given every 6–8 h	Eosinophilia	/1	/42	/X	/6	/<1	/X
Ceftriaxone	IV	50–75 mg/kg/d, divided into doses given every 12 h or single daily dosing	Diarrhea, eosinophilia; contraindicated in neonates with hyperbilirubinemia	2/<1	24/12	X/X	4/2	0/<1	40/31
Cefixime	Oral	<45 kg, 8 mg/kg given once daily; >45 kg, 400 mg given once daily	Abdominal pain, diarrhea, flatulence, indigestion, loose stool, nausea						
Ceftazidime	IV	30–50 mg/kg given every 8 h	Diarrhea, rash	2/<1	33/15	X/X	4/2	<1/<1	10/4
Ciprofloxacin	Oral, IV	10–20 mg/kg given orally every 8 h (maximum 750 mg/dose); 6–10 mg given IV every 8 h (maximum 400 mg/dose)	Tendonitis, tendon rupture Pediatric patients at risk for adverse events related to joints	9/5	1/1	12/5	4/3	6/3	11/5

Table 6-4 (*continued*)

Antibiotic	Oral or IV	Dose	Side Effects and Contraindications	Inpatient and Outpatient Uropathogen Percentage Antibiotic Resistance (%)					
				Escherichia coli	*Entero-bacter*	*Entero-coccus*	*Klebsiella*	*Proteus mirabilis*	*Pseudomonas aeruginosa*
Broad-spectrum Antibiotics (*continued*)									
Piperacillin/ tazobactam	IV	300 mg/kg/d divided into doses given every 6–8 h	Rash	/1	/7	/X	/3	/<1	/5
Imipenem	IV	25 mg/kg given every 6 h (maximum 4 g/d)	Diarrhea, rash, nausea, vomiting, anemia	/<1	/<1	/X	/<1	/2	/3
Aztreonam	IV	30 mg/kg given IV every 8 h	Increased creat-inine and liver enzyme levels	/<1	/13	/X	/3	/<1	/4

Abbreviations: G6PD, glucose-6-phosphate dehydrogenase; IV, intravenous; TMP-SMX, trimethoprim-sulfamethoxazole; X, antibiotic resistance data not obtained for uropathogens known to not be susceptible. A blank value indicates that antibiotic was not tested for resistance in these studies.

Antibiotic resistance data adapted with permission from Edlin RS, Shapiro DJ, Hersh AL, Copp HL. Antibiotic resistance patterns of outpatient pediatric urinary tract infections. *J Urol.* 2013;190(1):222–227; and Saperston KN, Shapiro DJ, Hersh AL, Copp HL. A comparison of inpatient versus outpatient resistance patterns of pediatric urinary tract infection. *J Urol.* 2014;191(5 Suppl):1608–1613.



Abbreviations: Abx, antibiotics; cath, catheterization; cx, urine culture; dip, urine dipstick; IV, intravenous; po, oral; RBUS, renal/bladder ultrasonography; SPA, suprapubic aspiration; UA, urinalysis; UTI, urinary tract infection; VCUG, voiding cystourethrogram
*Increased likelihood in uncircumcised male, suprapubic tenderness, and temperature > 40°C.
**Consider ampicillin and third-generation cephalosporin or aminoglycoside in young infants. Use regional antibiograms.
***Higher risk for anatomic abnormalities with abnormal prenatal sonogram, previous febrile UTI, family history of genitourinary abnormalities, atypical organisms.
****Increased likelihood if previous UTI, dysuria, abdominal/flank tenderness.

Figure 6-7. Evaluation and treatment of the pediatric urinary tract infection.

Management After a Pediatric Urinary Tract Infection

The goal after treatment of a UTI is to prevent further UTIs. Approximately 10% to 30% of children will develop at least one recurrent UTI. After confirmation of a febrile UTI, parents should be instructed to seek prompt medical evaluation and care for future febrile illnesses, in an effort to prevent renal damage. The AAP recommends that all infants who have sustained a febrile UTI should have a urine specimen obtained at the onset of subsequent febrile illnesses so that a UTI can be diagnosed and treated promptly. Primary care providers should routinely monitor height, weight, and blood pressure in children with a history of a febrile UTI. Additionally, it is paramount for providers to identify and address risk factors that can predispose the patient to urinary stasis, such as anatomic abnormalities and voiding dysfunction. Bladder and bowel dysfunction should be considered as a potential contributing factor in the evaluation of all pediatric UTIs, and a thorough voiding history is essential in all children who are toilet trained. Recurrent UTIs are estimated to occur in 45% of children with bladder and bowel dysfunction, as opposed to 15% without it. Additionally, there is a well-recognized link between bladder dysfunction, VUR, and renal injury. Anorectal and lower urinary tract function are interrelated, and constipation occurs with bladder dysfunction 30% to 88% of the time. Treatment of constipation has been shown to reduce recurrent UTIs and improve bladder function. Initial measures to treat bladder and bowel dysfunction include modification of voiding behaviors with timed voiding and treatment of constipation. Clinical improvement after treating a UTI is sufficient to confirm successful treatment. In general, test of cure by performing repeat urine cultures to check for treatment success is not warranted, as long as there has been clinical improvement and/or resolution of the patient's initial symptoms.

There is debate regarding the effectiveness of prophylactic antibiotics for the prevention of recurrent UTIs, as well as valid concerns regarding antibiotic resistance and other systemic side effects in children. The role of prophylaxis is clearer in those at high risk for recurrent UTI, such as girls with dilating VUR with a history of febrile UTIs. The following characteristics are associated with a low risk of recurrent UTI, thus reducing the likelihood of benefit from prophylaxis in children with these traits: circumcised boys, normal RBUS or DMSA scan findings, lack of anatomic abnormalities, and non-dilating VUR. In the prospective Randomized Intervention for Vesicoureteral Reflux (RIVUR) trial,

TMP-SMX prophylaxis was compared with placebo in 600 children with grades I to IV VUR after UTI and showed that those on prophylaxis had a significantly reduced risk of recurrent UTI. Risk reduction was greatest in those with bowel and bladder dysfunction at baseline, a history of febrile UTI, or high grades of VUR.

When to Refer

- Recurrent afebrile, symptomatic UTIs and/or recurrent febrile UTIs
- UTIs not responsive to initial antibiotic therapy
- Febrile UTI in an infant
- Abnormal RBUS and/or VCUG findings
- Prenatally known or postnatally diagnosed congenital genitourinary anomaly, such as posterior urethral valve, VUR, hydronephrosis, ureteropelvic junction obstruction, bladder or urethral abnormalities, or genital abnormalities
- Known or suspected spinal dysraphism
- Concern for bowel and bladder dysfunction not improving with treatment of constipation and behavioral management, such as voiding symptoms of incontinence, dysuria, enuresis, frequency, and urgency without a UTI

Clinical Pearls

- Signs and symptoms of UTI, especially in infants, can be vague and nonspecific. Always keep UTI in your differential diagnosis for a febrile infant.
- UTIs are more common in girls, except during the first year after birth.
- Uncircumcised boys are 10 times more likely than their circumcised counterparts to have a UTI in the first 6 months after birth.
- A true UTI requires demonstration of bacteria in the urine and symptoms.
- Increasing episodes of pyelonephritis and delay in antibiotic treatment increase the risk of renal scarring and renal damage, so it is important to prevent recurrent febrile UTI, as well as institute antibiotic therapy early in the clinical course.
- Most of the time, pyelonephritis is associated with fever, nausea, vomiting, or flank pain.

- Do not rule out a concurrent UTI, even if a potential source of fever has been identified.
- Asymptomatic bacteriuria (without concurrent anatomic abnormalities) does not require screening or antibiotic treatment.
- Urine samples from a bag or diaper pad are only helpful when they have negative findings.
- Leukocyte esterase and nitrites on urine dipstick and bacteria on Gram stain are good rapid screening tests for UTI.
- Urine culture is necessary to establish a diagnosis of UTI. Both overtreatment and undertreatment of UTIs can lead to poor patient outcomes.
- RBUS is a noninvasive, relatively inexpensive way to screen for urinary tract abnormalities in a patient with a history of febrile UTI, but when used in isolation it may lead to VUR being missed.
- VCUG should be performed if RBUS findings are abnormal and/or if the UTI is atypical. Its use sooner can be tailored to the individual.
- Narrow-spectrum antibiotics are preferred for empirical UTI treatment, if possible.
- Uncomplicated cystitis can usually be treated with a 2- to 4-day antibiotic course, while febrile UTI and pyelonephritis in children should be treated with a 7- to 14-day course.
- In nontoxic patients older than 2 months who can tolerate oral intake, pyelonephritis can be managed as an outpatient, as long as parent compliance is not in question.
- All children with a history of UTI should be assessed for bladder and bowel dysfunction. Treatment of voiding dysfunction and constipation decreases recurrent UTIs and promotes resolution of VUR.

Resources for Parents

- US Department of Health and Human Services, National Institute of Diabetes and Digestive and Kidney Diseases. Bladder infection (urinary tract infection—UTI) in children. https://www.niddk.nih.gov/health-information/urologic-diseases/urinary-tract-infections-in-children. Accessed October 16, 2018
- KidsHealth. Infections. Urinary tract infections. http://kidshealth.org/en/parents/urinary.html. Reviewed May 2016. Accessed October 16, 2018

- American Academy of Pediatrics. Detecting urinary tract infections. HealthyChildren.org Web site. https://www.healthychildren.org/English/health-issues/conditions/genitourinary-tract/Pages/Detecting-Urinary-Tract-Infections.aspx. Updated November 21, 2015. Accessed October 16, 2018
- American Academy of Pediatrics. Prevent urinary tract infections in children. HealthyChildren.org Web site. https://www.healthychildren.org/English/health-issues/conditions/genitourinary-tract/Pages/Prevent-Urinary-Tract-Infections-in-Children.aspx. Updated November 21, 2015. Accessed October 16, 2018
- American Academy of Pediatrics Section on Urology. Recurrent urinary tract infections (UTIs) in children. HealthyChildren.org Web site. https://www.healthychildren.org/English/health-issues/conditions/genitourinary-tract/Pages/Urinary-Tract-Infections-in-Teens.aspx. Updated May 23, 2018. Accessed October 16, 2018

Suggested Readings

Copp HL, Yiee JH, Smith A, Hanley J, Saigal CS; Urologic Diseases in America Project. Use of urine testing in outpatients treated for urinary tract infection. *Pediatrics*. 2013;132(3):437–444

Foxman B. Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *Am J Med*. 2002;113(1 Suppl 1A):5S–13S

Glissmeyer EW, Korgenski EK, Wilkes J, et al. Dipstick screening for urinary tract infection in febrile infants. *Pediatrics*. 2014;133(5):e1121–e1127

Hay AD, Sterne JAC, Hood K, et al. Improving the diagnosis and treatment of urinary tract infection in young children in primary care: results from the DUTY prospective diagnostic cohort study. *Ann Fam Med*. 2016;14(4):325–336

Koff SA, Wagner TT, Jayanthi VR. The relationship among dysfunctional elimination syndromes, primary vesicoureteral reflux and urinary tract infections in children. *J Urol*. 1998;160(3 Pt 2):1019–1022

La Scola C, De Mutiis C, Hewitt IK, et al. Different guidelines for imaging after first UTI in febrile infants: yield, cost, and radiation. *Pediatrics*. 2013;131(3):e665–e671

Hoberman A, Greenfield SP, Mattoo TK, et al; RIVUR Trial Investigators. Antimicrobial prophylaxis for children with vesicoureteral reflux. *N Engl J Med*. 2014;370(25):2367–2376

Shaikh N, Morone NE, Lopez J, et al. Does this child have a urinary tract infection? *JAMA*. 2007;298(24):2895–2904

American Academy of Pediatrics Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. *Pediatrics*. 2011;128(3):595–610

Toffolo A, Ammenti A, Montini G. Long-term clinical consequences of urinary tract infections during childhood: a review. *Acta Paediatr*. 2012;101(10):1018–1031

Wan J, Skoog SJ, Hulbert WC, et al; American Academy of Pediatrics Section on Urology Executive Committee. Section on Urology response to new guidelines for the diagnosis and management of UTI. *Pediatrics*. 2012;129(4):e1051–e1053

CHAPTER 7

Voiding Dysfunction and the Wet Child

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Introduction

Urinary incontinence and voiding dysfunction are extremely common medical conditions among children. One study showed that up to 15% of chief complaints among patients who present to pediatricians were related to urinary function—often to incontinence. While some have historically been dismissive of its physical effects on patients, largely out of the belief that few, if any, untoward pathologic problems arise from urinary incontinence, it is now recognized that if left untreated, urinary incontinence and enuresis contribute to lower self-esteem, increased anxiety and social isolation, increased economic burden on families, and disrupted family dynamics. In many cases, first-line therapy in a neurologically normal child consists of behavioral modification to unlearn poor urinary (and bowel) habits and reinforce healthy ones. Enuresis may, in some instances, signify underlying anatomic or pathologic abnormality, which should prompt referral to a specialist. To make an informed determination, a full understanding of the wet child, including differential diagnosis, standardized terminology, and treatment options, are crucial to the practicing pediatrician. This chapter will cover common terms defined by the International Children's Continence Society and basic principles of incontinence, enuresis,

and voiding dysfunction, as well as current evidence-based treatment options for the primary care provider.

Terminology

The umbrella term *bowel and bladder dysfunction* is used to describe common coexisting symptoms related to the gastrointestinal and urinary tracts. *Bowel and bladder dysfunction* does not suggest etiologic origin or pathogenesis but is clinically descriptive of children who present with disturbances of the bowel (eg, constipation) and bladder (eg, incontinence).

Urinary symptoms can be divided into 2 broad categories: storage and voiding symptoms. Storage symptoms include alterations in frequency, feelings of urgency, and incontinence or the involuntary loss of urine. Urinary frequency can be decreased (≤3 voids per day), normal (4–7 voids per day), or increased (≥8 voids per day). *Urinary urgency* describes a sudden and compelling need to void and may be associated with incontinence. Increased urinary frequency and urgency are signs of bladder overactivity. Parents may associate urgency and frequency with urinary tract infection (UTI), but these symptoms are nonspecific and should be placed in the context of a complete history, physical examination, and workup to make such a determination. Finally, incontinence can be classified in several ways, including continuous versus intermittent, daytime versus nighttime, and primary versus secondary. Continuous incontinence, when elicited from patients or families, is often associated with an anatomic abnormality such as ectopic ureter. Intermittent incontinence is generally related to functional voiding problems. *Enuresis* refers to involuntary loss of urine while sleeping and more commonly occurs at night but can occur during the day, at nap time. Primary disorders relate to incontinence or enuresis present since toilet training, whereas secondary disorders arise after at least a 6-month period without involuntary loss of urine.

When enuresis occurs only at night without other daytime urinary symptoms, this is termed *monosymptomatic enuresis* (MSE). If there are daytime symptoms or wetting during the day and night, this is referred to as *nonmonosymptomatic enuresis* (NMSE). The reason for this dichotomy is not arbitrary but, importantly, relates to both treatment options and outcomes. Other common terms used to describe voiding symptoms include *dysuria* (pain or discomfort with urination), *straining*

(requiring increased effort and abdominal pressure or Valsalva to expel urine), *weak stream*, *hesitancy* (difficulty starting urination), and *intermittency* (urinary stream that starts and stops).

Giggle incontinence is the involuntary loss of urine during laughter. This is a specific form of voiding dysfunction related to bladder overactivity where laughter, coughing, or sneezing triggers a detrusor contraction. This is believed to be more common in girls than boys. Ninety-five percent of patients with giggle incontinence have concomitant daytime voiding symptoms, and treatment should be directed at these symptoms.

Incontinence is only considered pathologic in patients 5 years and older. Many patients achieve voluntary control of the urinary tract prior to this age and, variably, there are other contributors to the maturational process, including developmental level and presence of behavioral disorders.

Prevalence

Voiding dysfunction is extremely common among pediatric patients. In one study, investigators noted that among a control population who presented to primary care providers, 15% of patients came specifically for a urinary problem. When asked specifically about other urinary problems, 22% of all patients presenting to these providers noted either daytime urinary symptoms or nocturnal enuresis. Longitudinal studies have showed that 15% of 5- and 7-year-olds have enuresis. This decreases about 15% per year until age 15, when fewer than 1% still report episodes of nocturnal enuresis. In children, as the frequency of nocturnal enuresis episodes per night increases, the risk of daytime symptoms increases as well. About one-third of children with enuretic episodes of 2 or more nights per week have daytime symptoms. By definition, these children have the more-difficult-to-treat NMSE.

Populations with select comorbid conditions, such as sickle cell anemia, history of posterior urethral vales, and cerebral palsy, have increased risk of enuresis as high as 25%. Similarly, there is a strong overlap in nearly one-third of enuretic patients with behavioral conditions such as attention-deficit/hyperactivity disorder, conduct disorder, and oppositional defiant disorder. Successful treatment requires that these issues also be addressed.

Pathophysiology

Enuresis is believed to result from a delay in maturation, with arguments supporting this noting the high spontaneous resolution rates as patients get older. While maturational delay is likely involved, its explanation is multifactorial, including maladaptive behaviors. Three organ systems have been implicated in patients with enuresis: kidney, brain, and bladder. Normal circadian release of antidiuretic hormone (or arginine vasopressin) from the posterior pituitary gland is greater at night, thus decreasing urine production with increased concentration of urine. Some children with enuresis do not have this normal increased release of vasopressin and, thus, have nocturnal polyuria that overwhelms baseline functional bladder capacity, leading to loss of urine. Diminished sleep arousal may also play a key role in enuresis, causing children to ignore signals of a full bladder. Finally, patients with small bladders or decreased functional capacity will be at risk for developing enuresis.

Bowel dysfunction, if present, is believed to contribute strongly to voiding dysfunction as a result of the shared neural pathways and close proximity to the bladder in the pelvis. Bowel and bladder dysfunction is also believed to be multifactorial in nature, developing as a result of maladaptive behaviors, including holding and postponement of urination or defecation. Dietary factors can also strongly influence bowel and bladder function, including poor fluid intake, low fiber intake, or intake of caffeine, artificial sweeteners, and other bladder irritants.

Diagnosis and Evaluation

History

Complete workup of a patient with incontinence or voiding dysfunction begins with a thorough patient history. While the subject matter at hand is sensitive, maintaining an open, encouraging, and objective approach to patients helps to remove stigma in the eyes of the patient regarding bowel and bladder problems. The practitioner should inquire about the presence of symptoms attributable to lower urinary tract function, including storage symptoms such as urgency, frequency, or incontinence. Timing of incontinence should be clarified (continuous vs intermittent, day vs night, how often). Secondary enuresis (or new

incontinence after a period of at least 6 months of being dry) should prompt questions about changes in daily activities or new stressors at home or school.

Similarly, history of recent bowel activity is necessary to determine if there is concomitant bowel dysfunction. Constipation as a concept confuses many parents and providers because there are not great definitions for constipation, and the definition of functional constipation and/or bowel dysfunction remains controversial. Simply asking if a patient has constipation is often insufficient; rather, providers should delve more specifically into bowel movement frequency, fecal soiling, abdominal pain, size of stool, and consistency of bowel movements according to a reference such as the American Academy of Pediatrics Bowel Movement Chart [**Figure 7-1**]). To frame the questions, it is helpful to note that patients, as a goal, should have a soft, smooth, daily bowel movement that is easy to expel without pain, as depicted in **Figure 7-1**.

Patients who present with bowel and bladder dysfunction or enuresis should be encouraged to fill out a bowel and bladder diary to obtain an objective appreciation for elimination habits (**Figure 7-2**). This diary should span 7 days and nights, noting times of voids, bowel movements, associated stool consistency as noted on the bowel movement chart, and any episodes of incontinence during the day or at night. This will provide a more complete picture, and one that is free of recall bias. For patients with a primary complaint of voiding dysfunction, a 48-hour frequency-volume chart can be obtained. This is usually done on a weekend for family convenience, and it consists of recording volumes of fluid intake and voided urine and the presence of any episodes of incontinence. This can help determine whether there is increased (or decreased) urinary frequency, define functional bladder capacity (usually defined as largest void during the day in the diary), determine whether polyuria is playing a role, and even tease out dietary habits that are contributing to overall voiding dysfunction (eg, intake of caffeinated beverages or large intake of fluids prior to bedtime). Normal bladder capacity in children is estimated with the following equation: estimated bladder capacity (in mL) = (age in years + 2) × (30 mL).

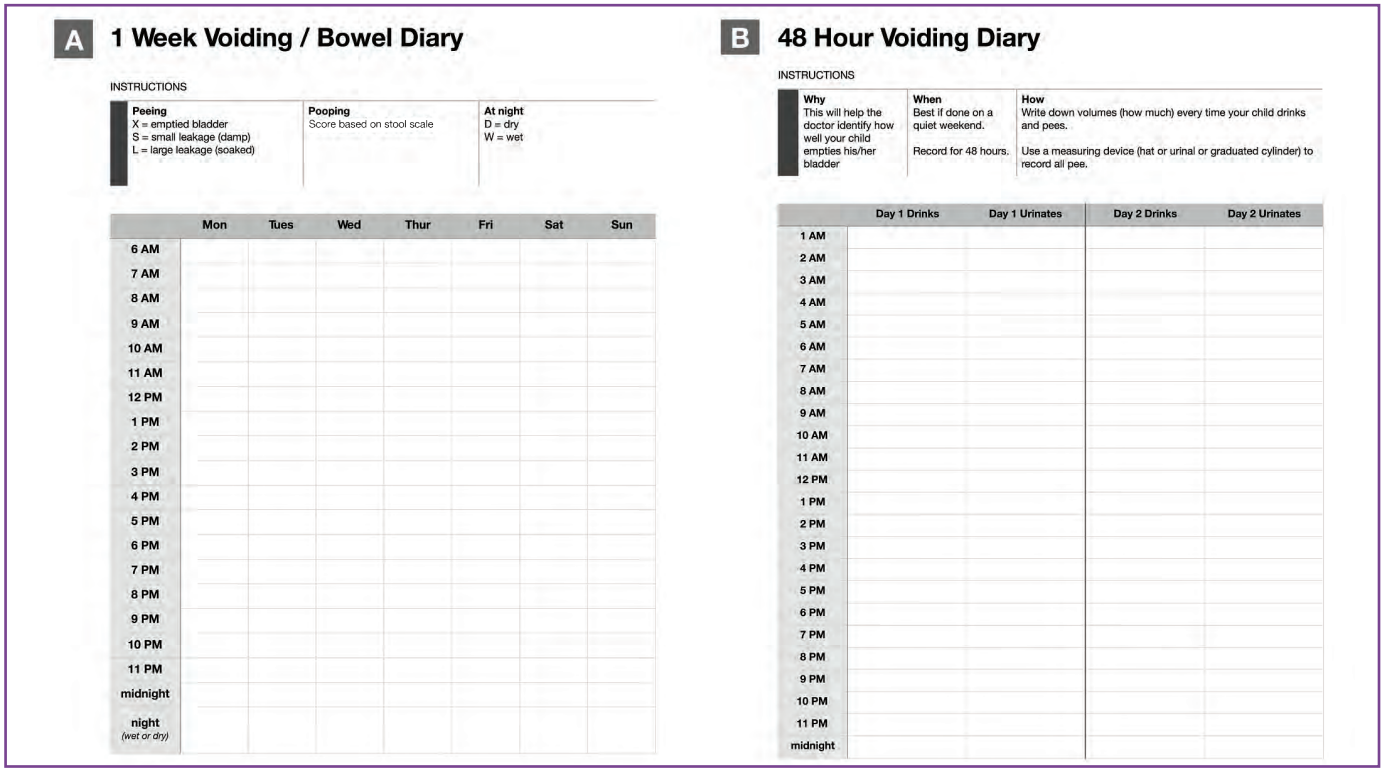
As with questions related to bowel function, parents may not be attuned to subtle but pathologic voiding habits, and diaries are a great method to clarify these details.

American Academy of Pediatrics Bowel Movement Chart[a]			
What type of BM does your child have?	**What does it look like?**	**How often is your child having a BM?**	**Can your child tell you if it comes out easily?**
Hard (Constipation)	Hard pebbles	Daily or not often	Doesn't come out easily and is painful
	Short, compact chunks; may look bumpy	Daily or not often	Doesn't come out easily and may be painful
Normal	Soft tube shape; can have slight bumps or uneven surface	Daily or every other day	Comes out easily
Soft or loose	Separate blobs with no defined shape that can be easily mushed	Daily or multiple times per day May leak out of a diaper	Comes out easily
Watery (Diarrhea)	Liquid with no clumps	Every few hours or more Will most likely leak out of a diaper	Comes out easily, but your child may feel burning

Abbreviation: BM, bowel movement.

[a] Applies to children who are older than 12 months and whose main source of nutrients is no longer formula or breastfeeding.

Figure 7-1. The American Academy of Pediatrics Bowel Movement Chart.



A 1 Week Voiding / Bowel Diary

INSTRUCTIONS

Peeing	Pooping	At night
X = emptied bladder S = small leakage (damp) L = large leakage (soaked)	Score based on stool scale	D = dry W = wet

	Mon	Tues	Wed	Thur	Fri	Sat	Sun
6 AM							
7 AM							
8 AM							
9 AM							
10 AM							
11 AM							
12 PM							
1 PM							
2 PM							
3 PM							
4 PM							
5 PM							
6 PM							
7 PM							
8 PM							
9 PM							
10 PM							
11 PM							
midnight							
night (wet or dry)							

B 48 Hour Voiding Diary

INSTRUCTIONS

Why	When	How
This will help the doctor identify how well your child empties his/her bladder	Best if done on a quiet weekend. Record for 48 hours.	Write down volumes (how much) every time your child drinks and pees. Use a measuring device (hat or urinal or graduated cylinder) to record all pee.

	Day 1 Drinks	Day 1 Urinates	Day 2 Drinks	Day 2 Urinates
1 AM				
2 AM				
3 AM				
4 AM				
5 AM				
6 AM				
7 AM				
8 AM				
9 AM				
10 AM				
11 AM				
12 PM				
1 PM				
2 PM				
3 PM				
4 PM				
5 PM				
6 PM				
7 PM				
8 PM				
9 PM				
10 PM				
11 PM				
midnight				

Figure 7-2. A, Example of a 1-week voiding and bowel diary. Patients are separately provided with a pictographic stool scale for reference. **B,** Example of a 48-hour frequency and volume chart that provides greater detail about liquid intake and urinary output.

With girls, asking about posture while voiding on the toilet is also relevant. Slouching while sitting on the toilet, sitting on the edge of the toilet with feet barely touching the floor, or sitting with legs together all promote tightening of the pelvic floor musculature. This, in turn, leads to increased bladder outlet resistance and higher voiding pressures and may contribute to urinary symptoms such as dysuria or incomplete emptying, subsequently increasing the risk of bladder dysfunction or UTIs. Proper posture on the toilet should be encouraged and, if needed, a footstool can be used (**Figure 7-3**).

In some circumstances, the child has been encouraged to sit on the toilet "backwards," facing the tank, thus necessitating the legs being

Figure 7-3. Proper posture on the toilet is demonstrated, with support for the feet if necessary. Avoid dangling the feet over the edge of the toilet, as this likely increases the pelvic floor muscle tone, inhibiting relaxation for voiding.

apart and minimizing poor posture. Holding maneuverers, posturing, leg crossing, squatting, and grabbing of the perineum are commonly witnessed in children who are attempting to postpone urination in response to bladder spasms (resulting from either a full bladder or overactivity). These maneuvers increase perineal pressure and inhibit bladder contractions through a sacral reflex arc.

History of UTI should be discussed, as well as whether these were associated with fevers. Culture-documented UTI may indicate some level of urinary stasis or incomplete bladder emptying, as well as structural abnormalities such as vesicoureteral reflux or obstruction. Urinary symptoms such as pain, dysuria, urgency, and frequency may lead patients or families to believe a UTI is present. Some families may believe that their children have had "UTIs" in the past, on the basis of recurrent symptoms from voiding dysfunction, in the presence of sterile urine. When a urinalysis is performed, pyuria, hematuria, and debris may be found without bacteria, reflecting chronic inflammation and irritation of the urothelium. It is important for the practitioner to differentiate true infection from the symptoms to better direct therapy. As per the definitions laid out earlier, enuretic patients with irritative voiding symptoms such as cystitis in the absence of a positive urine culture result are treated as having NMSE and not MSE.

Finally, as a part of the medical history, screening for neurological symptoms should be performed, asking about change in gait, perineal numbness, altered sensorium of the extremities, or new problems with coordination. These might point to occult neurological disease, such as a tethered spinal cord, that requires further workup and management, particularly in the setting of secondary enuresis.

Physical Examination

For patients who present with bowel and bladder dysfunction, a physical examination with a genitourinary examination should be performed. Relevant findings to each portion of the examination are discussed herein.

Abdominal examination should include visualization to note the presence of distention that might indicate underlying bowel dysfunction. All 4 quadrants should be palpated to look for masses or palpable hard stool in the colon (usually only felt in extreme cases of constipation and may be more appreciable in small children). Tenderness to palpation

and/or fullness of the suprapubic area may indicate urinary retention or a full bladder.

Neurological assessment of reflexes, strength, coordination, and sensation of all extremities should be performed. The spine should be visualized and palpated to rule out occult neurological issues that might arise with bony vertebral or sacral abnormalities. If present, these should be investigated further. Skin changes such as sacral dimple, abnormal-appearing gluteal cleft, or lipoma or hair tuft should also be investigated, as these may signify the presence of occult spinal dysraphism or tethered cord (**Figure 7-4**).

Genitourinary examination should include inspection of the genitalia to look for evidence of damp underwear or external genital irritation, which can occur with incontinence. In the male, the penis should be inspected and examined, including circumcision status, evidence of balanitis, foreskin swelling, or redness. If circumcised, meatal stenosis should be noted. Meatal stenosis occurs only in male patients who have been circumcised. Importantly, a physical examination finding of stenosis is only believed to be relevant in the context of a clinical history of

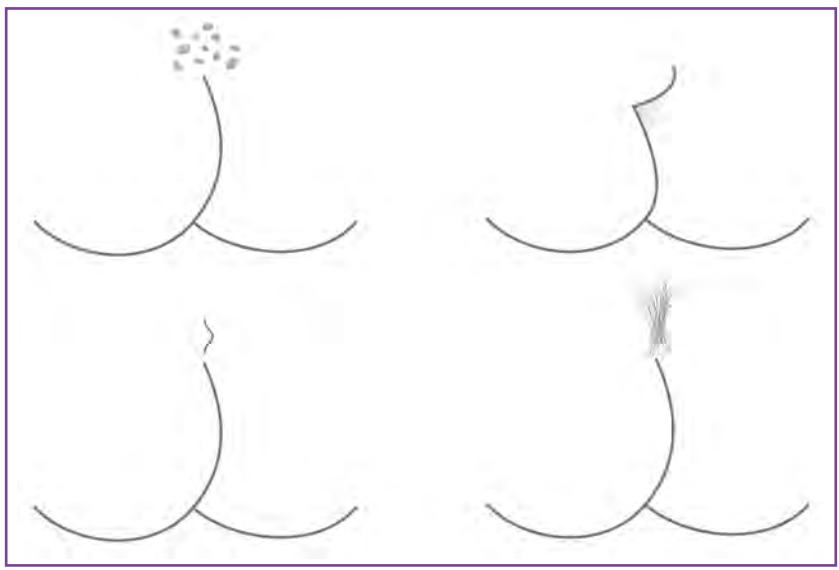


Figure 7-4. Skin changes over the spine that are suspicious for spina bifida, including isolated macules (top left), deviated cleft (top right), soft protuberance (bottom left), and isolated tuft of hair (bottom right).

narrow and/or deviated stream that is difficult to direct into the toilet. Together, this should prompt referral to a specialist for possible intervention. While there may be voiding symptoms associated with this examination finding, they typically persist after correction of the stenosis and should be treated separately. In the female patient, the vaginal introitus should be examined for pooling of urine or irritation. If there is continuous incontinence, the child may have an ectopic ureter that inserts below the urethral sphincter, allowing for continuous dribbling (**Figure 7-5**).

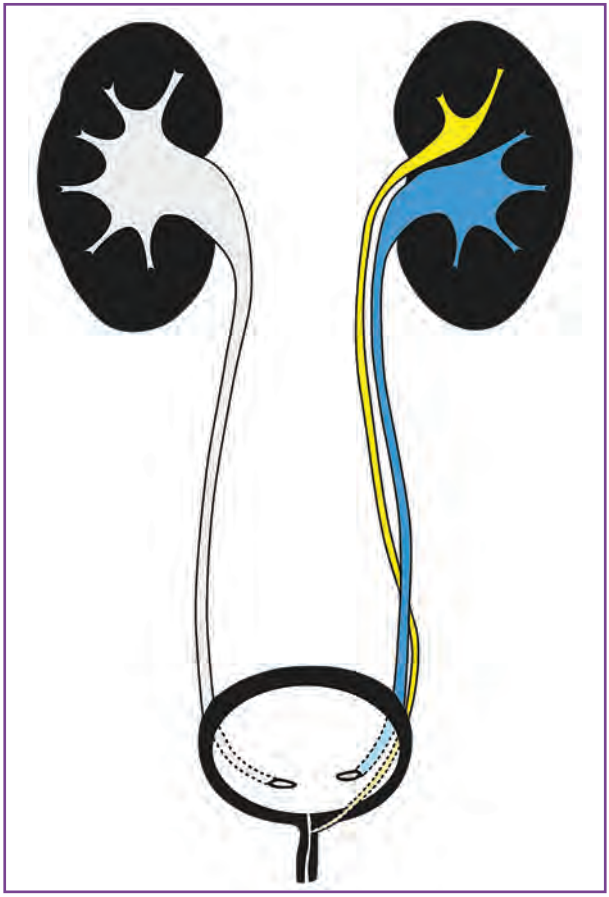


Figure 7-5. Schematic of the kidneys, ureters, and bladder with complete duplication on one side. The orientation of the duplex ureters is governed by the Weigert-Meyer rule. In this case, the ectopic upper pole ureter inserts below the bladder neck (yellow). In a female patient, this would likely produce continuous incontinence.

Additional Testing

Urinalysis and culture should be performed if there are irritative voiding symptoms (dysuria, urgency, or frequency) to rule out the presence of untreated UTI. If symptoms persist in light of an appropriately treated infection or negative culture finding, treatment should be directed toward voiding and bowel dysfunction.

Some of the noninvasive testing discussed here may fall under the purview of specialist providers, such as pediatric urologists, but the primary care provider should be aware of their utility. Pre- and postvoid ultrasonography of the pelvis can typically be performed in the office, if a machine is available. This allows for a quick, noninvasive, and nonionizing method of visualization of the bladder and rectum. A thickened bladder wall may be seen, indicating increased work of the detrusor during emptying secondary to increased outlet resistance or increased pelvic floor muscle tone; debris within the bladder is sometimes seen if there is urinary stasis or ongoing inflammation or infection and can provide an estimate of voiding efficiency and calculation of postvoid residual volume. Further, if there is a large stool ball in the rectum, this can be easily seen with ultrasonography (**Figure 7-6**). Rectal diameter larger than 30 mm in a child without the urge to defecate is suggestive of bowel dysfunction.

Uroflowmetry is a measurement typically performed with a uroflowmeter, a device used to measure the rate of fluid passed into it. Patients void into the machine, and it generates a curve that helps visualize the voiding pattern (normal is bell shaped and abnormal is flat, interrupted, or staccato in appearance), total volume voided, time spent voiding, and average and maximum flow rates. All of these variables are interpreted in the context of a clinical history to determine voiding efficiency and best treatment course. **Figure 7-7** provides examples of normal and abnormal flow patterns.

Treatment Options and Outcomes

NMSE (and bowel and bladder dysfunction) are treated differently than MSE. Namely, focus is placed on eliminating daytime symptoms through conservative management, treating underlying constipation and bowel dysfunction, addressing any behavioral and psychological

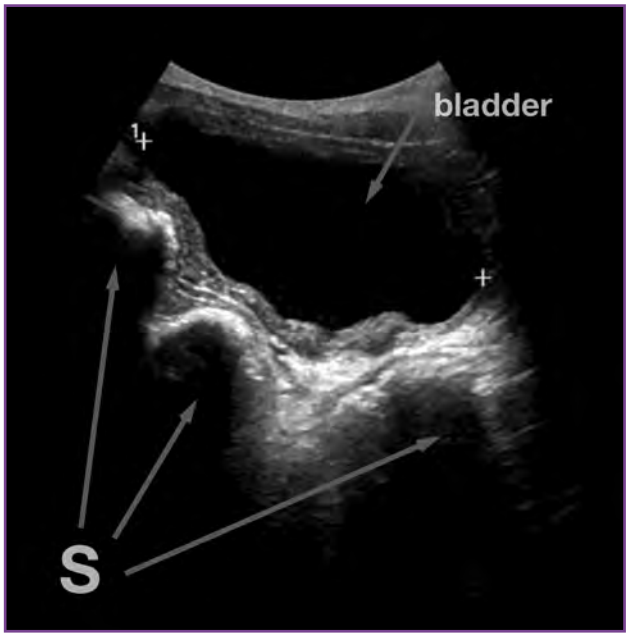


Figure 7-6. Large stool balls posterior to the bladder are denoted by the *S* seen in the rectum and are distorting the shape of the bladder. These are prominent and visible at pelvic ultrasonography.

problems, and then determining if nocturnal enuresis still persists. If it does, then and only then does one proceed with standard MSE therapies (which are discussed further herein).

Urotherapy and Conservative Management

Urotherapy is a conservative behavioral modification therapy that should be first-line therapy for any new patient who presents with daytime voiding dysfunction. Education of the child and family is key, including addressing poor bowel and bladder habits. Providing written information with an educational handout that explains easy methods to achieve normal bowel function encourages regular and prompt emptying of the bladder and avoidance of postponement. Handing out the voiding diaries discussed earlier is also useful. Timed voiding (voiding on a schedule of every 2–3 hours) for patients with infrequent, large voids or those who empty incompletely is recommended, as is avoidance of bladder irritants in the diet (**Box 7-1**).

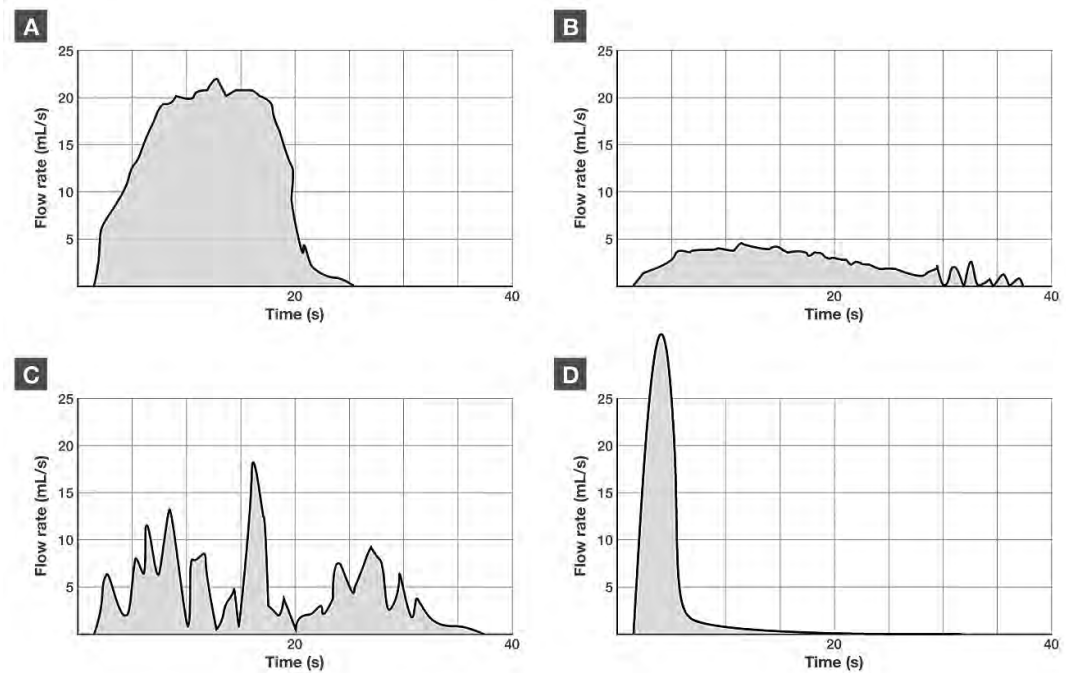


Figure 7-7. **A,** Example of a uroflowmetry printout for a normal patient with a bell-shaped curve. Total volume is usually recorded, and a minimum of approximately 100 to 150 mL is needed to qualitatively assess urine flow pattern. **B,** Obstructive flow pattern. **C,** Overactivity pattern resembles staccato or flow starting and stopping. **D,** Peaked flow pattern with rapid emptying of the bladder may cause turbulence and possible symptoms during urination.

Box 7-1. Possible Bladder Irritants in the Diet
Common Bladder Irritants
Caffeine (coffee, tea)
Sports drinks
Carbonated beverages
Chocolate
Spicy foods (onions, tomatoes, chilies, peppers)
Artificial sweeteners
Some fruits and their juices (oranges, lemons, pineapple)

The authors typically recommend that patients drink plenty of water and avoid items on this list. Patients who regularly consume more than 1 item on the list may try cutting out 1 item at a time, to see if that particular item is contributing to symptoms.

Posture should be addressed. Child-friendly diaries can be used as a reward chart, with places for stickers for each void. In the authors' practice, parents fill out a weeklong diary during the first week after their initial visit to provide baseline information and then repeat this at 6 and 12 weeks to monitor progress. Most children experience improvement with behavioral modification. Patients who do not respond may require specialized intervention or may have a neurological component. Referral for further evaluation should be considered.

More advanced forms of urotherapy, often instituted by pediatric urological specialists and trained nursing urotherapists, include biofeedback and pelvic floor physical therapy. Biofeedback is a method of retraining the pelvic floor musculature through a device connected to electromyography (EMG) patch leads to the perineal muscles. Feedback on the device allows the user to become familiar with, coordinate, and relax these muscles during voiding. Physical therapy similarly focuses on pelvic floor relaxation techniques. Notably, physical therapy for incontinence in the pediatric patient is different than in adult female patients, who are more likely to have stress urinary incontinence, which improves with exercises to tighten the pelvic floor. In a child, this might worsen symptoms, so tightening (Kegel) exercises should be avoided.

Constipation Management

Treating constipation is critical for improving urinary symptoms. As mentioned earlier, many parents do not consider their child "constipated," but when asked more specific questions, many patients with bowel and bladder dysfunction have underlying, subclinical constipation. As with voiding dysfunction, family education is a cornerstone. A soft, smooth daily bowel movement that is easy to expel without pain is the goal. First-line therapy to achieve this includes increased water or fluid intake and increased fiber in the diet. Second-line therapies include oral fiber supplementation and/or an oral osmotic laxative such as polyethylene glycol, titrated to effect. For more severe cases, bowel clean-out protocols and even fecal disimpaction may be needed, and consultation with gastroenterology specialists is recommended.

Despite multiple attempts at conservative therapy and trials of appropriate medications to target urological symptoms (see the Advanced Therapies section), patients may need to be referred for formal urodynamics. Patients with high postvoid residual volumes, recurrent UTIs, or other refractory daytime symptoms may require more invasive testing. Formal urodynamics involve placing catheters in the bladder and rectum and EMG electrodes on the perineum to measure pressures, bladder response, and urinary sphincter function as the bladder is filled with either saline or contrast material. Urodynamics can provide more insight into the function of the lower urinary tract in patients with complex presentations.

Advanced Therapies

α-Blockers are a class of medications that antagonize smooth-muscle α-adrenergic receptors found in the bladder neck. Relaxation of the bladder neck will result in more complete bladder emptying in children who fail to relax normally during voiding. Some patients with voiding dysfunction who have evidence of functional bladder outlet obstruction may benefit from this class of medications. Selective α-blockers such as tamsulosin minimize systemic effects such as postural hypotension and have been shown to improve coordination of voiding. In the United States, it should be noted that these medications are not approved by the U.S. Food and Drug Administration (FDA) for this indication. It should be disclosed to families that therapeutic use in children for voiding dysfunction is off-label.

More recently, β_3 receptor agonists (eg, mirabegron) have been introduced and approved for adults with overactive bladder. β_3 receptors are found in the smooth muscle of the bladder, and their activation results in bladder wall relaxation. β_3 receptor activation has been studied in children and shown improvement in overactive bladder symptoms. As yet, no formal FDA indication for use in children has been given.

Botulinum toxin A is another medication with approval for use in adults with overactive bladder and problems related to a hypercontractile bladder. The medication is typically injected throughout the bladder via a cystoscope with the patient under general anesthesia, and the effect lasts 6 to 9 months on average. A small percentage of patients may have increased postvoid residual or even urinary retention that requires catheterization after injection. Its use in children with voiding dysfunction remains investigational with ongoing studies.

Enuresis-Specific Therapies

Behavioral modification should be used for first-line treatment of MSE or the patient with NSME with adequately treated daytime symptoms and persistent nocturnal enuresis. Behavioral modification can take several forms. Educate patients to refrain from drinking substantial amounts of fluids in the hour prior to going to bed. Patients should void prior to going to bed. There is some evidence that reward systems such as star charts are associated with fewer wet nights. Lifting is a behavioral treatment where a caregiver lifts the patient from bed while sleeping and takes him or her to the bathroom to allow urination in the correct location. Some have believed this to be counterproductive, as enuretic episodes occur randomly during all sleep stages. Scheduled wakening is another strategy that involves waking a child to get up and urinate prior to any accident. Punishment has also been studied and been shown to have a negative effect on outcomes.

Moisture or bed-wetting alarms are available commercially and, when used properly, two-thirds of patients became dry during therapy. This effect persists in 50% of patients after therapy has completed. The alarm works by stimulating the sleeping patient (with sound, light, and—historically—electric shock) and increases the relationship between a full bladder and arousal centers. This is believed to be a classic conditioning response. It has the highest success rate among all the different treatment modalities, but it requires a time investment by the family to

ensure success. Parents must participate and fully awaken the child during therapy and direct him or her to the bathroom to complete urination.

Desmopressin is an FDA-approved analogue of antidiuretic hormone (also known as *arginine vasopressin*) that increases expression of aquaporin receptors in the kidney to cause increased water resorption. There are no central effects; urine production decreases. Desmopressin is given 0.2 to 0.6 mg orally once daily before bedtime. Twenty percent to 30% of enuretic patients will become completely dry during therapy. Patients with nocturnal polyuria respond best to this medication (defined as patients who produce >130% of expected bladder capacity volume of urine during the night). The medication is safe. Patients should not drink in the hour prior to bedtime. The medication can be used nightly or as needed (eg, only for sleepovers or camping trips), when enuresis would be socially unacceptable. However, up to one-half of responders will begin to wet again after medication is stopped.

Imipramine is a tricyclic antidepressant that was first noted to improve enuresis. A recent meta-analysis shows that its use results in one fewer wet night per week on average, with 22% of patients becoming completely dry. It has multiple mechanisms of action, including an anticholinergic relaxing effect on the bladder wall, stimulation of the external urethral sphincter, and a central effect on enuresis that is not well understood. Like desmopressin, the therapeutic effect goes away once the medication is discontinued. Tricyclics are less effective than moisture alarms. Comparison to desmopressin amongst studies has shown similar effectiveness, but the side effects are negligible with desmopressin, which does not act centrally.

The bladder smooth muscle has cholinergic receptors. Anticholinergic medications (eg, oxybutynin, tolterodine) have been studied in randomized controlled trials for MSE as first-line therapy and have been shown to be ineffective. There is believed to be benefit in some patients with NMSE, because these patients may have detrusor overactivity or reduced functional capacity, both of which are improved with anticholinergic therapy. There may be a role for combination therapy with the addition of anticholinergics in patients who fail to achieve dryness with maximum doses of desmopressin.

Many other pharmaceutical therapies have been investigated, including diazepam, nonsteroidal anti-inflammatory medications, and amphetamines, among others. These generally have similar or decreased

effectiveness when compared with the drugs already presented and do not have FDA-approved indications for enuresis. A meta-analysis of complementary and other miscellaneous interventions, such as hypnosis and acupuncture, for enuresis similarly showed mixed evidence of varying, poor quality. A flowchart for the typical evaluation and treatment of patients with NMSE and MSE is provided (**Figure 7-8**).

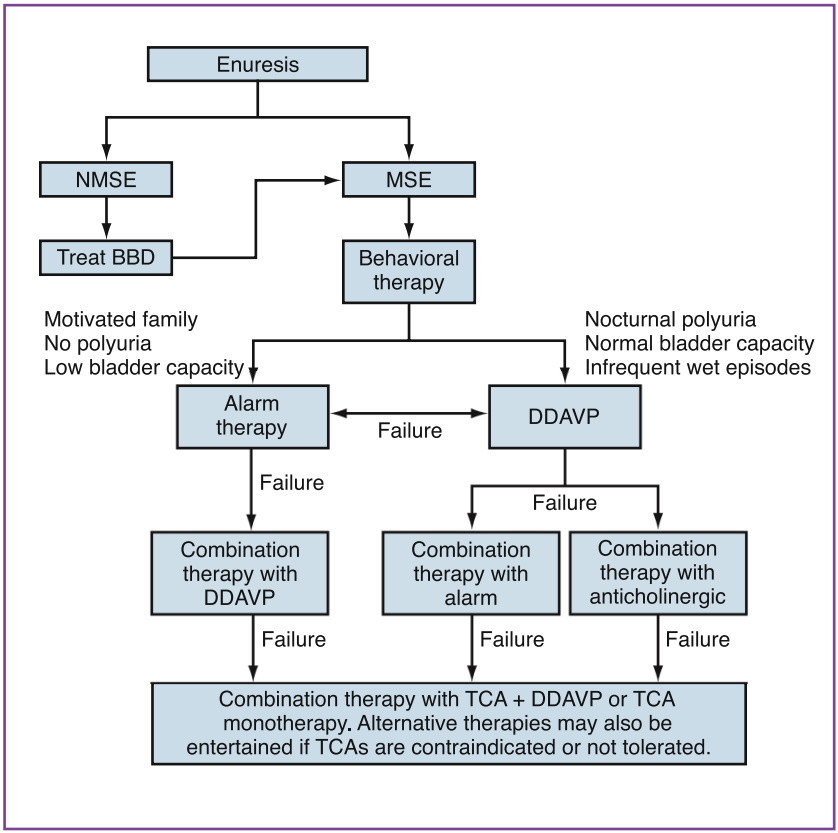


Figure 7-8. Algorithm for evaluation and treatment of a patient with enuresis. BBD, bowel and bladder dysfunction; DDAVP, 1-deamino-8-D-arginine vasopressin or desmopressin; MSE, monosymptomatic enuresis; NMSE, nonmonosymptomatic enuresis; TCA, tricyclic antidepressant.

Reprinted with permission from Austin PF, Vricella GJ. Functional disorders of the lower urinary tract in children. In: Wein A, Kavoussi LR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology*. 11th ed. Philadelphia, PA: Elsevier; 2016:3297–3316.

When to Refer

- Refer patients with continuous, primary incontinence that occurs during the day and at night.
- Constipation that is refractory to first- and second-line therapies should prompt further workup.
- Refer boys with clinically significant meatal stenosis (diverted urinary stream, prolonged time to empty bladder) with or without concomitant urinary symptoms.
- Refer patients with NMSE who have persistent daytime symptoms and in whom conservative therapies fail.
- Refer patients with incontinence (particularly secondary incontinence or wetness that is new after a period of 6 or more months of dryness) and positive neurological results on review of symptoms or physical examination findings.

Clinical Pearls

- Enuresis is found in 15% of 5-year-olds, and 15% of these children will experience spontaneous resolution each year.
- A complete elimination history, including bowel and bladder habits, is key to determining treatment course.
- Children with daytime voiding symptoms and nocturnal enuresis (NMSE) should be treated differently than patients with only nocturnal enuresis (MSE).
- Patients with NMSE should have bowel and bladder function addressed prior to any interventions for nighttime wetting.
- Primary interventions for both MSE and NMSE are usually conservative with behavioral modification.

Resources for Parents

- International Children's Continence Society. General public. http://i-c-c-s.org/parents. Accessed October 17, 2018
- Cincinnati Children's Hospital. Pediatric constipation. https://www.cincinnatichildrens.org/health/c/constipation. Updated July 2016. Accessed October 17, 2018

Suggested Readings

Dos Santos J, Varghese A, Williams K, et al. Recommendations for the management of bladder bowel dysfunction in children. *Pediatr Ther*. 2014;4:1–11

Nepple KG, Cooper CS. Etiology and clinical features of bladder dysfunction in children. UpToDate. https://www.uptodate.com/contents/etiology-and-clinical-features-of-bladder-dysfunction-in-children. Reviewed September 2018. Accessed October 17, 2018

Austin PF, Bauer SB, Bower W, et al. The standardization of terminology of lower urinary tract function in children and adolescents: update report from the Standardization Committee of the International Children's Continence Society. *J Urol*. 2014;191(6): 1863–1865.e13

References

Nevéus T, von Gontard A, Hoebeke P, et al. The standardization of terminology of lower urinary tract function in children and adolescents: report from the Standardisation Committee of the International Children's Continence Society. *J Urol*. 2006;176(1): 314–324

Austin PF, Bauer SB, Bower W, et al. The standardization of terminology of lower urinary tract function in children and adolescents: update report from the Standardization Committee of the International Children's Continence Society. *J Urol*. 2014;191(6): 1863–1865.e13

Bauer SB, Austin PF, Rawashdeh YF, et al; International Children's Continence Society. International Children's Continence Society's recommendations for initial diagnostic evaluation and follow-up in congenital neuropathic bladder and bowel dysfunction in children. *Neurourol Urodyn*. 2012;31(5):610–614

Forsythe WI, Redmond A. Enuresis and spontaneous cure rate. Study of 1129 enuretis. *Arch Dis Child*. 1974;49(4):259–263

Franco I, von Gontard A, De Gennaro M; International Children's Continence Society. Evaluation and treatment of nonmonosymptomatic nocturnal enuresis: a standardization document from the International Children's Continence Society. *J Pediatr Urol*. 2013;9(2):234–243

Roth EB, Austin PF. Evaluation and treatment of nonmonosymptomatic enuresis. *Pediatr Rev*. 2014;35(10):430–436, quiz 437–438

Oliver JL, Campigotto MJ, Coplen DE, Traxel EJ, Austin PF. Psychosocial comorbidities and obesity are associated with lower urinary tract symptoms in children with voiding dysfunction. *J Urol*. 2013;190(4 Suppl):1511–1515

Chase J, Austin P, Hoebeke P, McKenna P; International Children's Continence Society. The management of dysfunctional voiding in children: a report from the Standardisation Committee of the International Children's Continence Society. *J Urol*. 2010;183(4):1296–1302

Burgers RE, Mugie SM, Chase J, et al. Management of functional constipation in children with lower urinary tract symptoms: report from the Standardization Committee of the International Children's Continence Society. *J Urol*. 2013;190(1):29–36

Vricella GJ, Campigotto M, Coplen DE, Traxel EJ, Austin PF. Long-term efficacy and durability of botulinum-A toxin for refractory dysfunctional voiding in children. *J Urol*. 2014;191(5 Suppl):1586–1591

CHAPTER 8

Vesicoureteral Reflux

Saul P. Greenfield, MD, FAAP, FACS

Introduction

Vesicoureteral reflux (VUR) is the regurgitation of urine back up the ureter toward the kidney. Reflux is prevented by a "flap valve" mechanism in the region of the bladder base, where the ureter enters the bladder (**Figure 8-1**). As the bladder fills with urine, the ureter is compressed to

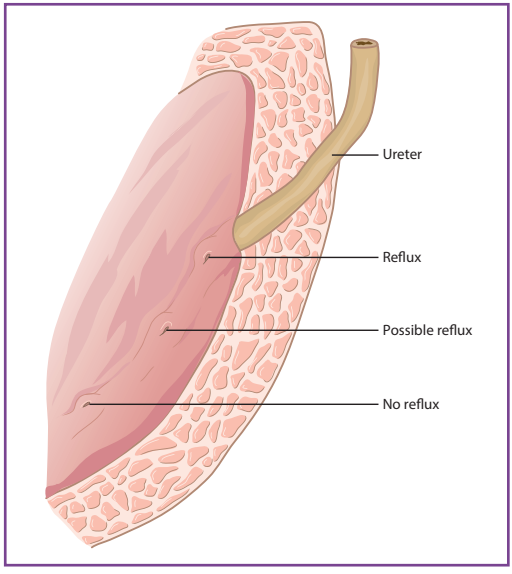


Figure 8-1. Anatomic configuration of normal and abnormal vesicoureteral junction.

prevent reflux. This "flap valve" mechanism will fail to prevent reflux if the "tunnel" of the ureter is too short as it traverses the bladder wall. In addition, abnormally high pressures of voiding may overcome a structurally normal valve mechanism. *Primary reflux* is the failure of this ureteral tunnel to develop properly and is congenital. *Secondary reflux* may be caused by disorders of bladder function that result in abnormally high bladder pressures, which overcome a normal valve, and is most often not present at birth. Primary VUR occurs in less than 1% of the general population.

In the 1990s, approximately 50,000 new cases of reflux were diagnosed per year in the United States. Reflux is diagnosed and graded with voiding cystourethrography (VCUG), wherein the awake child is catheterized and the bladder is filled with contrast material via gravity drip. Reflux is diagnosed if contrast material is seen going up the ureters, toward the kidneys. Images are obtained during filling and voiding. It is important that the child is awake and can void, since not all reflux is seen with passive filling of the bladder. Recently, the means by which VCUG should be performed have been standardized, so that studies are ideally comparable from different institutions.

Based on the appearance of the images, VUR is categorized from minimal to severe by using a 5-point grading system, known as the "International Scale" (**Figures 8-2** and **8-3**) Approximately 90% of

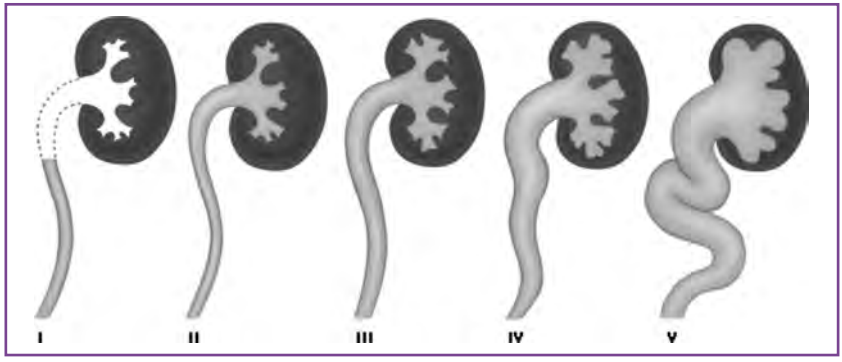


Figure 8-2. Schematic drawing of the 5 grades of vesicoureteral reflux. Grades I, II, and III are the most common.

Reprinted with permission from Keren R, Carpenter MA, Hoberman A, et al. Rationale and design issues of the Randomized Intervention for Children With Vesicoureteral Reflux (RIVUR) study. *Pediatrics.* 2008;122(Suppl 5):S240–S250.

Figure 8-3. Contrast-enhanced voiding cystourethrogram shows bilateral grade IV reflux.

children have low-grade (grade I, II, or III) reflux. Renal ultrasonography (US) cannot be used to diagnose reflux and findings are most often within reference range, even with high-grade (grades IV and V) reflux. Many children with reflux have spontaneous resolution and are considered to have "outgrown" the reflux.

Diagnosis

Since the 1960s, primary, congenital VUR has been recognized as a major cause of morbidity in pediatric populations. Most children are discovered to have reflux after a urinary tract infection (UTI). Up to 50% of all children who present with their first UTI will have reflux. VUR is associated with recurrent nonfebrile and febrile UTI, either cystitis or pyelonephritis. Children with reflux do not efficiently empty their urinary tracts of all urine along with bacteria, and this is thought to predispose children to UTIs. This is especially true of girls, whose

short urethra allows for easier entry of bacteria into the bladder, as well as uncircumcised boys, who have colonization of bacteria under the prepuce.

In the absence of infection, reflux is asymptomatic and is not perceived by the patient. Furthermore, sterile reflux is not harmful to the kidneys. A major morbidity of reflux is renal scarring or so-called reflux nephropathy. These scars are the result of pyelonephritis and can therefore only occur if the urine is infected. Some children with high-grade reflux appear to have "scarred" or dysmorphic kidneys from birth, before any urinary infections have occurred. It is believed that these children have renal hypoplasia or dysplasia, which is a congenital accompaniment of the highest grades of reflux in some newborns. Renal scarring is assessed most accurately and reliably by using radionuclide renal scanning (**Figure 8-4**).

Renal scars can cause hypertension in childhood or adulthood, and, if extensive and bilateral, they can be the cause of renal insufficiency. The worst cases result in end-stage renal disease and renal transplantation. Reports from the 1960s and 1970s, when reflux was less frequently recognized, demonstrated that pyelonephritic scarring was the etiologic origin of up to 50% of the cases of hypertension and up to 30% of cases of end-stage renal disease in children. These rates have been considerably reduced in contemporary populations, as a result of widespread recognition and treatment of VUR. Finally, reflux in adult women of

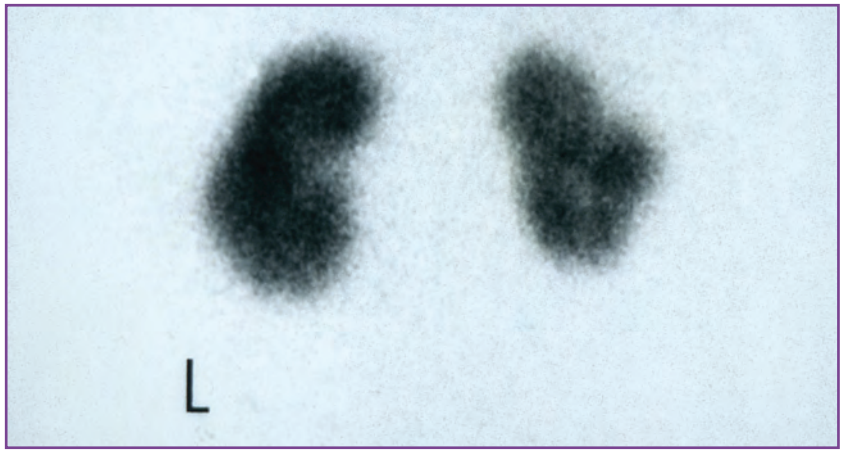


Figure 8-4. Technetium 99m dimercaptosuccinic acid renal scan shows clinically significant renal scarring.

childbearing age has been associated with increased rates of UTI and pyelonephritis during pregnancy. This can be the cause of preterm birth and fetal loss, if not recognized.

Evaluation

While primary VUR is most often diagnosed after a UTI, there are other modes of presentation. Reflux is hereditary and autosomal dominant, with variable penetrance. Approximately one-third of asymptomatic siblings will be found to have reflux, once the proband is identified. It had been recommended, therefore, to screen asymptomatic siblings with VCUG. This recommendation remains controversial. Some authorities will only screen younger siblings up to 4 or 5 years of age, since VUR is known to spontaneously improve over time. Others will only screen those with a history of infection. In any case, families should be counseled regarding the possibility of VUR existing in siblings. Again, most cases of reflux will be missed with renal US; it is *not* a substitute for screening with VCUG.

Fetal hydronephrosis, now often detected due to the common practice of prenatal US screening, is another means of diagnosing reflux. Approximately 25% of neonates with a prenatal US finding of a hydronephrotic kidney will be found to have reflux. Newborns identified in this manner can also be screened with VCUG shortly after birth. Again, some might follow these newborns expectantly to see if a UTI develops before performing VCUG; however, parents should be counseled regarding the probability of VUR. If it is anticipated that medical care for the child might not be reliable or continuous, early screening with VCUG would eliminate doubt about the presence of VUR.

Recently, the need to perform VCUG after the initial UTI in children of all ages has been questioned. Both the American Academy of Pediatrics and the United Kingdom–based National Institute for Health and Care Excellence published guidelines suggest that VCUG only be performed after more than 1 urinary infection—unless a renal US finding is abnormal or the child was septic. In contrast, others have shown that renal US findings are most often normal, even with high-grade VUR, and counter that many infants and children with VUR will be missed unless evaluated after the first UTI. If a VCUG is not elected after the first infection, families should be advised to return for urological evaluation

immediately if another infection is diagnosed. The social situation should also be assessed and considered, since families who are poorly compliant, who have limited access to health care, or who are mobile might be best evaluated with VCUG after a first documented infection.

Treatment Options and Outcomes

The principal goal is to prevent reflux-associated urinary infection—either symptomatic cystitis or febrile pyelonephritis—as well as renal scarring and progressive renal injury. Certain basic principles have emerged from decades of clinical research. These principles can be summarized as follows:

- VUR of any grade is harmless to kidneys, unless associated with urinary infection.
- Most children outgrow the lower grades of reflux (grade I, II, or III), but it is a slow process that may not occur until adolescence. The reported rates of spontaneous resolution over time are 90% for grade I, 75% to 80% for grade II, 50% for grade III, 20% for grade IV, and 0% to 5% for grade V.
- Continuous low-dose antibiotic prophylaxis for many years will prevent urinary infection in most children with reflux, until it is outgrown.
- Continuous antibiotic prophylaxis is as effective as antireflux surgery in preventing infection-associated renal damage in any grade of reflux.
- Antireflux surgery is usually reserved for those who develop breakthrough infection while taking a prophylaxis regimen, those who are noncompliant with a prophylactic regimen, those with high-grade reflux (grades IV and V) who have little chance of outgrowing it, or those with all grades of reflux who have reached adolescence with persistent reflux who desire correction. An exception is made for neonates who receive a diagnosis of grade IV or V reflux shortly after birth, since they have a higher rate of resolution than older children with those grades. These neonates should initially be given antibiotics and observed for several years. As stated earlier, however, if grades IV or V persist beyond the age of 3 or 4 years, there is much less likelihood of resolution with growth. Most children discovered to have VUR are therefore placed on continuous, daily low-dose antibiotic prophylaxis and undergo VCUG every 1 to 2 years.

There is controversy regarding the length of time needed for continuous daily antibiotics in most patients with low-grade (grade I, II, or III) reflux as children get older—even if the reflux has not resolved. The rates of pyelonephritis and scarring are low in those with lower grades of reflux. In grades I, II, or III reflux, renal scarring rates are less than 20%. It is not possible, however, to predict in whom scars may occur. There is understandable reluctance to recommend a course of treatment that requires many years of antibiotic therapy, along with repetitive and uncomfortable radiographic evaluations, if the risk of morbidity is low. There are also concerns regarding cost, side effects, the emergence of community antibiotic resistance (see the Antibiotic Prophylaxis section), and the likelihood of long-term compliance in many families. Similarly, there is reluctance to recommend surgery for many children, despite its high success rate and elimination of the need for long-term medical care.

Antibiotic Prophylaxis

Antibiotics are given as a nightly dose to maximize urinary concentration overnight, when there might be more static, easily infected urine in the bladder. Antibiotics commonly prescribed include trimethoprim (TMP)-sulfamethoxazole (SMX), nitrofurantoin, or trimethoprim alone. These broad-spectrum antibiotics are manufactured generically and are relatively inexpensive, do not need refrigeration, and are available in liquid form. Allergies to sulfa drugs can occur but are relatively rare. Nitrofurantoin is also well tolerated but can cause gastric upset in some. The liquid preparation is unpleasant tasting to many, so the capsules are often provided. Parents can open up the capsules and place the powder in a favorite food. Nitrofurantoin may be associated with less vaginitis in girls. Neither of these 2 antibiotics are safe until after the age of 2 months; therefore, 12.5 to 25 mg/kg of ampicillin given once nightly is used in the immediate newborn period. Cephalosporins may also be used in early infancy.

Antibiotic prophylaxis can be maintained until a radiograph shows that the reflux has resolved. Breakthrough infection, defined as a positive urine culture while on prophylaxis, is relatively uncommon and occurs in approximately 10% of populations on prophylaxis. Most breakthrough infections occur in girls. Antibiotic resistance can occur, but the recently published Randomized Intervention for Children With

Vesicoureteral Reflux (RIVUR) study showed that long-term use of TMP-SMX remained effective over 2 years.

Compliance with a regimen of daily prophylaxis, repetitive urine cultures, and cystograms is a challenge. Reported compliance rates vary from 12% to 90%. There have been no methods demonstrated to improve compliance, and this remains a challenge for those embarking on many years of prophylaxis.

Boys with reflux, especially infants younger than 1 year who are not circumcised, are at a greater risk of urinary infection. While circumcision is not absolutely necessary, families should be made aware of this association, and elective circumcision should be offered. If breakthrough infections occur in the uncircumcised boy while on prophylaxis, a reasonable alternative to surgical correction of the reflux would be to continue prophylaxis after circumcision and observe the patient.

Can antibiotics be stopped after a certain age, even though reflux may not have resolved? There are conflicting data regarding the risk of renal scarring and age. There are studies that show that pyelonephritis and renal scarring can occur in older children. If discontinuation is elected, it would be safest in the older toilet-trained child, who can communicate the symptoms of cystitis or pyelonephritis. A family should have a track record of compliance and a stable social situation. Children with the lowest risk are those with low-grade VUR, without bowel and bladder dysfunction (see the Bowel and Bladder Dysfunction section), who have no renal scarring seen on a radionuclide renal scan and who have remained infection free, without breakthroughs, for a number of years on prophylaxis. The large National Institutes of Health–sponsored RIVUR study showed that while on prophylaxis, recurrent infection rates were one-half those on a placebo, demonstrating that prophylaxis was beneficial in preventing UTIs.

Bowel and Bladder Dysfunction

Children with neurologically normal development can demonstrate clinically significant lower urinary tract dysfunction. This is most often manifest in the toilet-training years. As children try to toilet train, they may hold their urine and bowel movements for an excessive amount of time. Some children do not appropriately relax their perineal sphincters while voiding or defecating. As a result, they are often constipated and do not empty their bladders completely. There are higher than normal

voiding pressures, since voiding occurs when the urinary sphincter is not appropriately relaxed. They also tend to have unstable, "hyperreflexic" bladders that contract at lower than normal volumes. So, in addition to urinary holding habits, they may have both day and nighttime wetting. Reflux—usually low-grade—may result, since higher than normal voiding pressures can overcome a competent or marginally competent valve. These children often have recurrent UTIs with or without reflux, along with urinary incontinence and fecal soiling. A bladder that does not empty well predisposes the child to infection, since bacteria are not expelled with each void. Children with bowel and bladder dysfunction and VUR form a special subset of children with reflux, most of whom are girls. It has been shown that these children have a higher incidence of breakthrough infection while on prophylaxis, more renal scarring, a lower incidence of spontaneous resolution with growth, and a higher failure rate after antireflux surgery. For this reason, it is believed that these children need to be identified and treated.

To identify children with bowel and bladder dysfunction, most pediatric urologists rely on an oral history and a toilet diary completed at home, as well as noninvasive flow studies. Bowel and bladder dysfunction can be assessed historically by means of questionnaire or toileting diary. In particular, families are queried regarding voiding frequency, urinary incontinence, constipation, and fecal soiling (**Figure 8-5**).

Noninvasive urodynamics—consisting of measuring urinary flow rate, sphincteric muscle electronic activity, and postvoid residual urine—are most often performed (**Figure 8-6**). Voiding dysfunction can also be confirmed by more formal invasive urodynamic testing, which is a means of assessing bladder muscle contraction and compliance, intravesical pressures, sphincteric function, and postvoid residuals.

Once bowel and bladder dysfunction is identified, many urologists will assign children a timed voiding regimen, laxatives, and stool softeners, if necessary. Anticholinergics may be added to that regimen—specifically oxybutynin—to reduce bladder muscle overactivity and, thereby, lower bladder pressures. Some studies support the wide use of anticholinergics, demonstrating that children so treated will resolve their reflux sooner and have fewer breakthrough infections. Common side effects of oxybutynin include dry mouth, heat intolerance, and worsening constipation.

Toileting Diary

- Make an "X" for each urination in the "**Urine**" column.
- Make an "X" for each urinary accident in the "**A**" column.
- Make an "X" for each bowel movement in the "**BM**" column.
- Make an "X" for each bowel accident in the "**S**" column.
- Mark the "Overnight" row "**Wet**" or "**Dry**" based on how they wake up that morning.

Date: _____ Date: _____

Time	Urine	A	BM	S	Time	Urine	A	BM	S
Overnight					**Overnight**				

Figure 8-5. A sample toilet diary sent home for parents to complete.

Surgical Techniques

Ureteral Reimplantation

Conventional open surgery requires a lower abdominal incision, a short hospitalization of 1 to 3 days, and, typically, a recuperative period of 1 to 2 weeks. Re-creation of the natural valve mechanism is accomplished by "reimplanting" the ureter or reconfiguring the entrance of the ureter into the base of the bladder. This can be accomplished by any number of techniques that all approach 100% success, especially in the lower

Figure 8-6. The setup for noninvasive urodynamics, measurement of urinary flow rates, and sphincteric relaxation during voiding and postvoid residual urine amounts.

reflux grades. Surgery can be either intravesical or extravesical, and both techniques have equally high success rates (**Figure 8-7**).

Reflux correction by this means is most often permanent. Children now often go home after 1 to 3 days of hospitalization. Children are kept on antibiotic prophylaxis until renal US performed around 6 weeks after the surgery confirms no evidence of obstruction. Some physicians continue prophylactic antibiotics until repeat VCUG demonstrates that reflux is no longer present; however, given the high success rate with the surgery, many assume reflux correction and forego further VCUG unless a child has a recurrent UTI.

In the past decade, a new approach to ureteral reimplantation has been pursued, using laparoscopic instrumentation along with robotics. This minimally invasive technique remains investigational and has not been widely adopted to date. There are obstacles of technology and equipment availability, cost, and a steep learning curve. Success rates up to 85% have been reported in multi-institutional studies, which is not nearly as high as the rate for the conventional technique.

Injectable Materials

The most recent innovation in the treatment of VUR is the use of injectable bulking agents to reconfigure the ureteral orifice, thereby preventing VUR. This treatment has the lowest morbidity rate, as it is

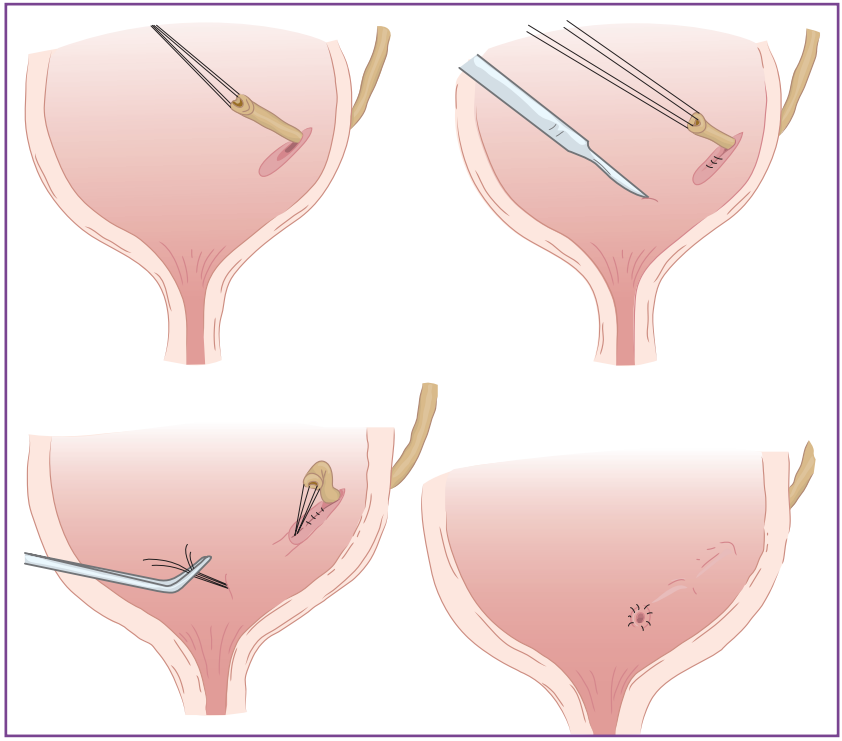


Figure 8-7. An example of an intravesical ureteral reimplantation, which restores the normal anatomic vesicoureteral junction and antireflux valve mechanism.

an ambulatory cystoscopic procedure performed with brief general anesthetic. There is virtually no postprocedural discomfort, and children return to full activity the next day.

The principle behind injection therapy is to reconfigure the ureteral orifice so that the valve becomes functional, preventing reflux (**Figure 8-8**).

Dextranomer/hyaluronic acid copolymer, or "dextranomer microspheres," have been introduced for use in the United States; they are currently the only agent with U.S. Food and Drug Administration approval for this purpose. The dextranomer microspheres are suspended in sodium hyaluronan. It is said to be nonimmunogenic, although rare foreign-body giant cell reaction has been reported. Size of the implant can decrease slightly over time, but the in-growth of fibroblasts stabilizes the volume of the implant. Success rates of up to 90% have been reported by some but average around 85%. Furthermore, 2 injections

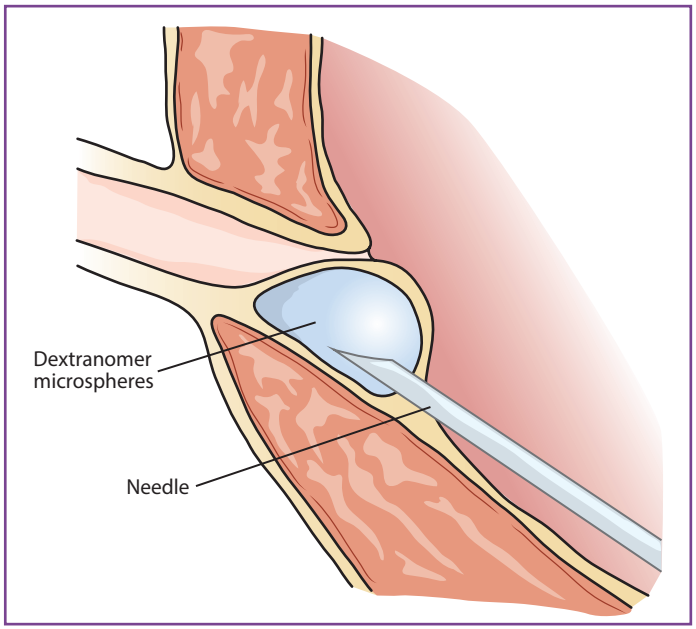


Figure 8-8. Injection of dextranomer microspheres, a "bulking" agent, which narrows the ureteral opening and can restore the antireflux function of the ureterovesical junction.

might be needed to achieve this level of success. Success may be less in high-grade (grades IV and V) reflux and in those with complete ureteral duplications. The dextranomer microspheres are not 100% durable, and despite early reflux correction, recurrent reflux, along with UTIs, has been reported. Rarely, late-developing ureteral obstruction can also occur.

A common protocol is to inject the dextranomer microspheres and then perform renal US and VCUG several months later. If reflux is still present, a second injection may be performed, followed by imaging studies—again, several months later. Alternatively, ureteral reimplantation may be performed in those with failed injection of dextranomer microspheres. Children can be taken off antibiotic prophylaxis after reflux is no longer present. Some authorities will not send children for imaging after injection of dextranomer microspheres but will reserve imaging for those who present with another UTI. Certainly, families need to be aware that repeat evaluation with VCUG may be needed if there is recurrent infection to see if reflux has recurred.

Given the low morbidity rate of this procedure, some families might prefer this intervention at the outset, without any trial of multiyear prophylaxis and repetitive VCUGs.

Current Practice

It is difficult to find uniform agreement as to what constitutes current best practice. The American Urological Association formed a guidelines panel that promulgated treatment recommendations based on a meta-analysis of the literature, and these were published in 2011. They acknowledged that there was not enough firm evidence to state definitive standards of care.

In general, ureteral reimplantation surgery is reserved for children older than 3 or 4 years with high-grade reflux (grades IV and V); those of any age with any grade, who are on prophylaxis and have breakthrough urinary infections; those with families who are not compliant with a medical regimen; those who may have achieved adolescent age without resolution; or those with families who desire correction.

Most other children are placed on low-dose antibiotic prophylaxis, as described earlier. VCUG is repeated every 1 to 2 years. Families should also be made aware of the surgical options—their advantages, disadvantages, morbidities, and success rates. Antibiotic prophylaxis can be stopped in an older toilet-trained child with persistent grade I or II reflux. This is safest for children who have no renal scarring, those who have had no breakthrough infections while on prophylaxis for a number of years, those who have families who are reluctant to let the child remain on long-term prophylaxis, and those who have a stable social situation at home.

When to Refer

Once reflux is identified, referral to a pediatric urologist depends on the ability and interest of the primary care practice to manage the child with low-grade (grades I, II, and III) reflux for the long-term. Children with grade IV or V reflux, however, are more often surgical candidates. If placed on antibiotic prophylaxis, the child may be followed up with periodic office visits to obtain urine cultures, monitor medication

adherence, and schedule repeat VCUG. Non–toilet-trained infants need to be catheterized for surveillance cultures. Bowel and bladder dysfunction should be assessed in the older toilet-trained child. Families should be aware of the possible involvement of asymptomatic siblings. Medical management by primary care physicians is, therefore, possible for those with lower grades of reflux, in whom spontaneous resolution is anticipated.

Indications for referral to pediatric urology include the following:

- Local practice of deferring management of long-term prophylaxis medications to a pediatric urologist or nephrologist
- Higher grades of reflux—grades IV and V
- Breakthrough urinary infection while on prophylaxis
- Families poorly compliant with long-term prophylaxis
- Family desire for surgical correction, along with reluctance to remain on prophylaxis and to undergo repetitive VCUG examinations
- Discussion of circumcision in uncircumcised boys with reflux
- Formal assessment of bowel and bladder dysfunction in the older toilet-trained child
- Review of VCUG to confirm grading and evaluation of VUR

Clinical Pearls

- Reflux is inherited but may be sporadic.
- Most low-grade (grades I and II) reflux resolves over time with somatic growth.
- Reflux is associated with recurrent urinary infection—both nonfebrile cystitis and pyelonephritis.
- Recurrent pyelonephritis and reflux can result in renal damage.
- Older toilet-trained children with reflux should be evaluated for bowel and bladder dysfunction.
- Circumcision should be considered in male infants with reflux and those with recurrent urinary infection.
- Surgical corrections—cystoscopic and open—have success rates ranging from 80% to 100%.
- Performing renal US alone will cause most cases of reflux to be missed, even those of the highest grades.
- Long-term antibiotic prophylaxis will prevent recurrent infection along with renal damage, unless there are breakthrough infections.

References

1. Greenfield S, Wan J. The diagnosis and medical management of primary vesicoureteral reflux. In: Gearhart J, Rink R, Mouriquand P, eds. *Pediatric Urology.* 2nd ed. Philadelphia, PA: Saunders Elsevier; 2010:301–321

2. Khoury A, Bagli D. Reflux and megaureter. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 9th ed. Philadelphia, PA: Saunders Elsevier; 2007:3423–3481

3. Hoberman A, Greenfield SP, Mattoo TK, et al; RIVUR Trial Investigators. Antimicrobial prophylaxis for children with vesicoureteral reflux. *N Engl J Med*. 2014;370(25):2367–2376

4. Carpenter MA, Hoberman A, Mattoo TK, et al; RIVUR Trial Investigators. The RIVUR trial: profile and baseline clinical associations of children with vesicoureteral reflux. *Pediatrics*. 2013;132(1):e34–e45

5. Peters CA, Skoog SJ, Arant BS Jr, et al. Summary of the AUA guideline on management of primary vesicoureteral reflux in children. *J Urol*. 2010;184(3):1134–1144

6. Frimberger D, Bauer SB, Cain MP, et al. Establishing a standard protocol for the voiding cystourethrography. *J Pediatr Urol*. 2016;12(6):362–366

CHAPTER 9

Congenital Hydronephrosis

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Introduction

Congenital hydronephrosis is commonly identified with prenatal ultrasonography (US) in up to 1% to 5% of fetuses. Although this finding reflects a spectrum of potential etiologic origins, it frequently causes unwarranted anxiety in parents and health care providers. The term *hydronephrosis* is descriptive, not diagnostic, and denotes water or urine ("hydro") in the kidney ("nephron"). A multidisciplinary consensus statement published by the Society for Fetal Urology (SFU) proposes replacing the term *hydronephrosis* with the term *urinary tract dilatation* (UTD). In up to 88% of cases (**Table 9-1**), UTD is not pathologic and resolves spontaneously.

In these cases, the UTD is thought to be caused by the increase in the fetal urine output in the latter half of the pregnancy. In the remainder, it may be secondary to an underlying urinary tract abnormality, and identifying this group of fetuses without over-investigating the vast majority of cases is an ongoing challenge. Various parameters have been used to predict the likelihood of pathologic findings: the renal pelvis anteroposterior (AP) diameter, the SFU grading system (in which the degree of calyceal dilatation and cortical thickness are considered, in addition to renal pelvic dilatation), and, most recently, the UTD classification,

Table 9-1. Etiologic Origins of Prenatally Diagnosed Urinary Tract Dilatation

Etiologic Origin	Incidence
Transient hydronephrosis	41%–88%
Ureteropelvic junction obstruction	10%–30%
Vesicoureteral reflux	10%–20%
Ureterovesical obstruction, megaureters	5%–10%
Ureterocele, ectopic ureter, duplex system	5%–7%
Multicystic dysplastic kidney	4%–6%
Posterior urethral valve, urethral atresia	1%–2%
Other: prune-belly syndrome, cystic kidney disease, congenital ureteric structures, megalourethra	Uncommon

Adapted with permission from Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). *J Pediatr Urol*. 2014;10(6):982–998.

which combines all these parameters with the presence of ureteric dilatation and amniotic fluid levels (**Figure 9-1**).

Babies born with an increased risk of underlying pathologic processes as a cause of UTD are routinely started on prophylactic antibiotics. In unilateral cases, initial imaging involves US performed when the baby is older than 48 hours, at which point the transient phase of oliguria after birth is complete, and US is more likely to demonstrate hydronephrosis or UTD from an obstructive cause. The timing of US is variable but is usually completed within the first month after birth. A more urgent evaluation is indicated where the prenatal UTD is bilateral or involves a solitary kidney. Further investigation and management will depend on the postnatal US findings and will be the focus of this chapter.

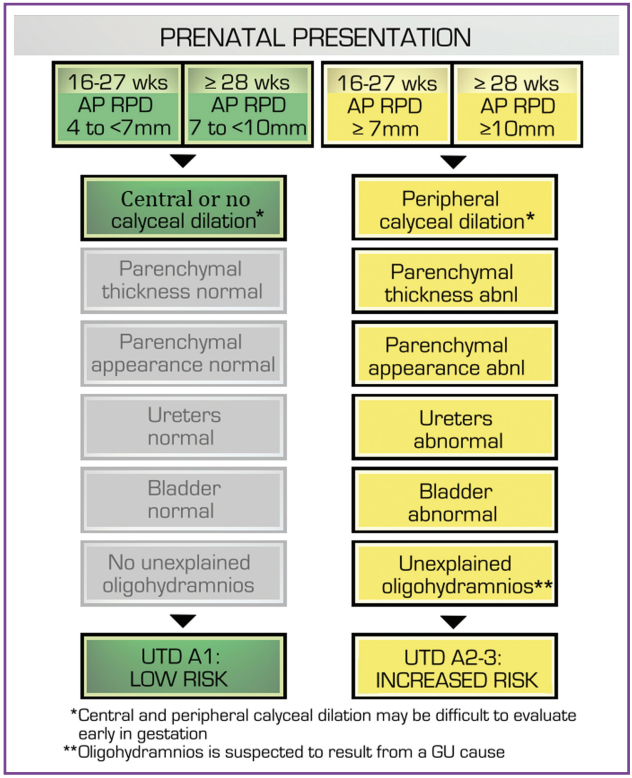


Figure 9-1. Prenatal urinary tract dilatation risk stratification.

Reprinted with permission from Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). *J Pediatr Urol.* 2014;10(6):982–998.

Ureteropelvic Junction Obstruction

Definition and Incidence

Ureteropelvic junction (UPJ) obstruction is defined as impaired urine flow from the renal pelvis into the proximal ureter, with subsequent dilatation of the collecting system and the potential for kidney damage. It leads to UTD without ureteric dilatation. The increase in pressure from the obstruction in the renal pelvis and calyces may result in subsequent damage to the nephrons, with loss of kidney function.

UPJ obstruction has an estimated incidence of 1 in 1,500 births. The left kidney is more commonly affected in a 2:1 ratio. Bilateral UPJ obstruction occurs in approximately 10% of cases. It is more common in children with other urinary tract anomalies and in association with congenital syndromes.

Etiologic Origin

UPJ obstruction can be caused by an intrinsic obstruction due to a short region of stenosis of unknown etiologic origin or an extrinsic obstruction by an aberrant crossing lower-pole vessel. The extrinsic cause is the most common cause of UPJ obstruction when it manifests symptomatically in childhood.

Diagnosis and Evaluation

Around 60% of cases of UPJ obstruction appear with prenatal UTD at presentation (**Figure 9-2A**). Alternative presentation occurs later in childhood or even in adults, with symptoms such as episodic flank pain often associated with nausea and vomiting, hematuria, urinary tract infections (UTIs), or an abdominal mass.

Suspected UPJ obstruction is investigated first with renal and bladder US, which typically demonstrates a dilated collecting system, including the renal pelvis and calyces. In addition, possible cortical thinning in the affected kidney with no ureteric dilatation beyond the region of the UPJ is a common US finding (**Figure 9-2B**). After identification of the dilated collecting system with US, a dynamic diuretic nuclear renogram, most commonly a technetium 99m (^{99m}Tc) mertiatide (MAG_3) renogram with furosemide, is obtained to assess the differential function of the 2 kidneys, as well as the washout or drainage of the dilated system after administration of furosemide (**Figure 9-3**).

Inconclusive studies may be confirmed intraoperatively by means of a retrograde pyelogram (**Figure 9-4**).

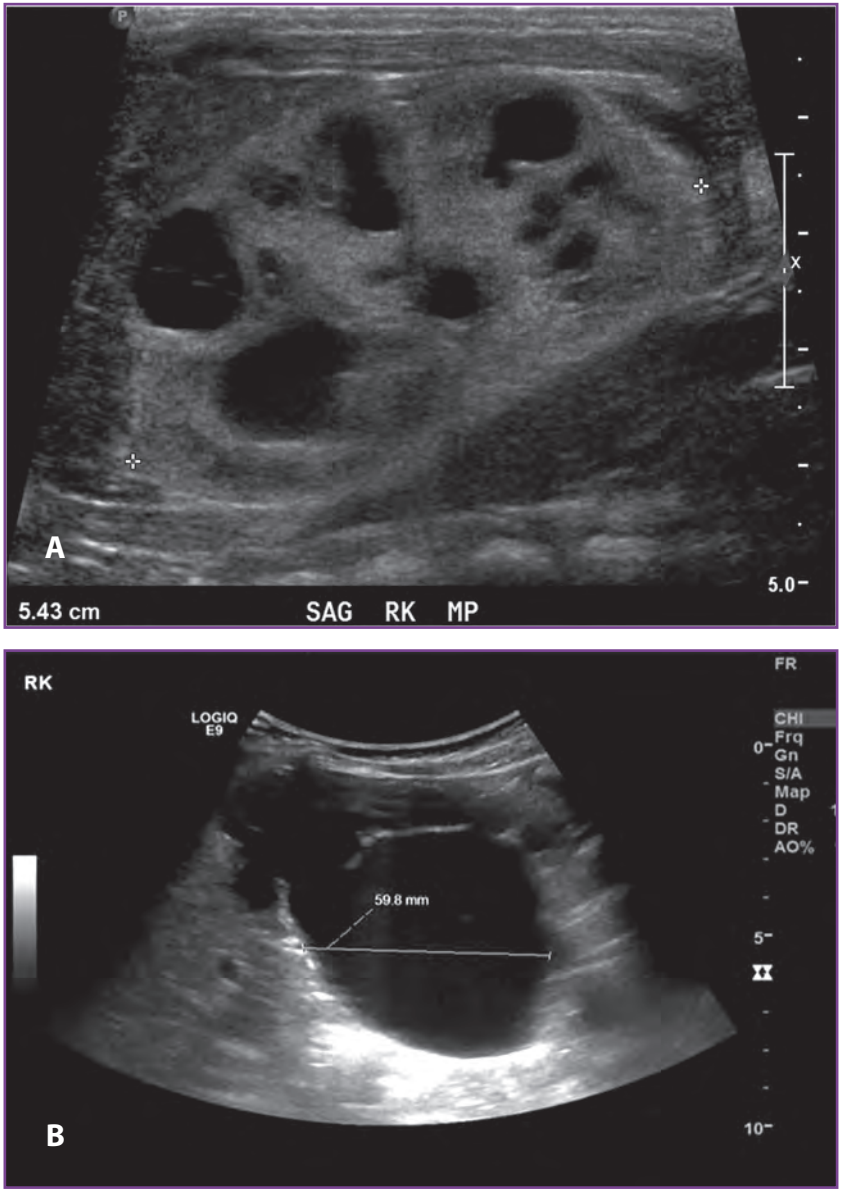


Figure 9-2. A, Prenatal ultrasonography (US) demonstrates hydronephrosis (dilated renal pelvis and calyces). **B,** Postnatal US demonstrates hydronephrosis with both renal pelvis and calyceal dilatation, as well as cortical thinning.

Figure 2A is from Feldenberg R, Beck A. Congenital diseases of the kidneys: prognosis and treatments. *NeoReviews*. 2017;18(6):e345–e356.

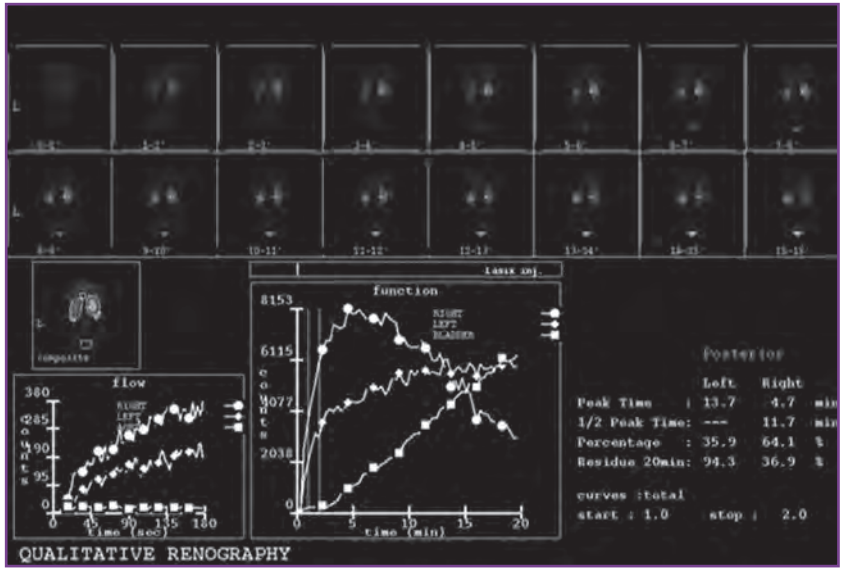


Figure 9-3. Technetium 99m mertiatide renogram demonstrates slow uptake of radiotracer and an obstructed drainage pattern of the left kidney (curve with diamonds), with reduced split function (35.9%). Of note, by convention, the images with nuclear renal scanning are from a posterior point of view.

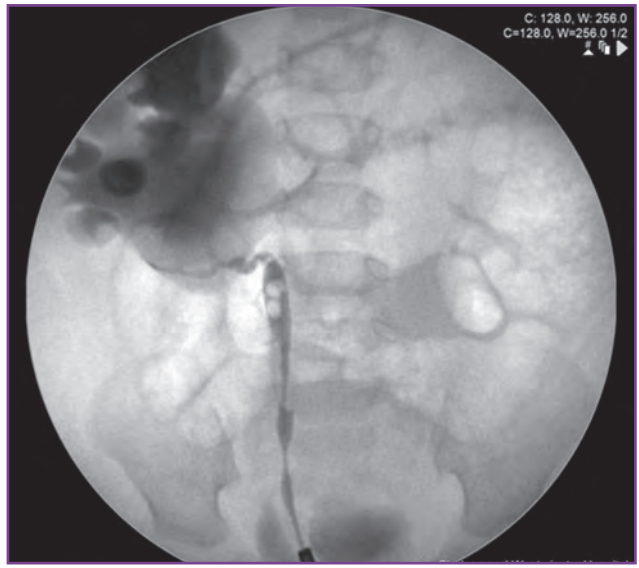


Figure 9-4. Intraoperative retrograde study demonstrates a dilated right renal pelvis with calyceal dilation and a tortuous, narrowed ureteropelvic junction.

Treatment Options and Outcomes

Conservative Management

In the prenatally diagnosed cohort, conservative management with serial imaging with US and/or renal scanning is undertaken when there is hydronephrosis associated with a normal differential renal function greater than 40%. When the dilatation is bilateral, less emphasis can be placed on the differential function, and management is guided by the severity of the dilatation and/or progression of dilation, which makes obstruction as the cause of the hydronephrosis more likely. In addition to serial imaging, daily antibiotic prophylaxis is frequently considered in those with severe UTD (AP diameter >15 mm) during the first 12 months after birth. Improvement in dilatation at serial renal US suggests spontaneous resolution, while increasing dilatation prompts a repeat nuclear renogram to reassess differential function and drainage. A decrease in the relative function when compared to the initial level of more than 5% is consistent with obstruction causing a progressive loss of function and is, therefore, an indication for surgical intervention. Surgery is usually performed shortly after diagnosis in those who present with symptoms later in life.

Surgical Management

Pyeloplasty is the procedure of choice for UPJ obstruction, and long-term success rates greater than 95% are expected, with a low incidence of recurrent obstruction. Indications for surgery include symptomatic UPJ obstruction (pain, hematuria, infection), asymptomatic obstruction with reduced function (<40%), or failure of conservative management (increasing dilatation or deteriorating functioning). The obstructing portion of the UPJ is excised, and an anastomosis is performed between the renal pelvis and normal ureter below the level of the obstruction. The procedure may be performed with an open incision or via laparoscopy, with or without robotic assistance. Postoperative follow-up consists of repeat US and/or MAG_3 renography.

Ureterovesical Junction Obstruction

Congenital anomalies of the ureterovesical junction (UVJ) often manifest prenatally with detection of a dilated ureter or "megaureter" (**Figure 9-5A**).

The ureter is sometimes not dilated enough to be routinely identified at prenatal US. A megaureter is defined as a ureteric diameter of 7 mm or larger after 30 weeks of gestation. Megaureters are classified into 4 categories: obstructed, refluxing, refluxing with obstruction, and non-refluxing and non-obstructing. UVJ obstruction has an

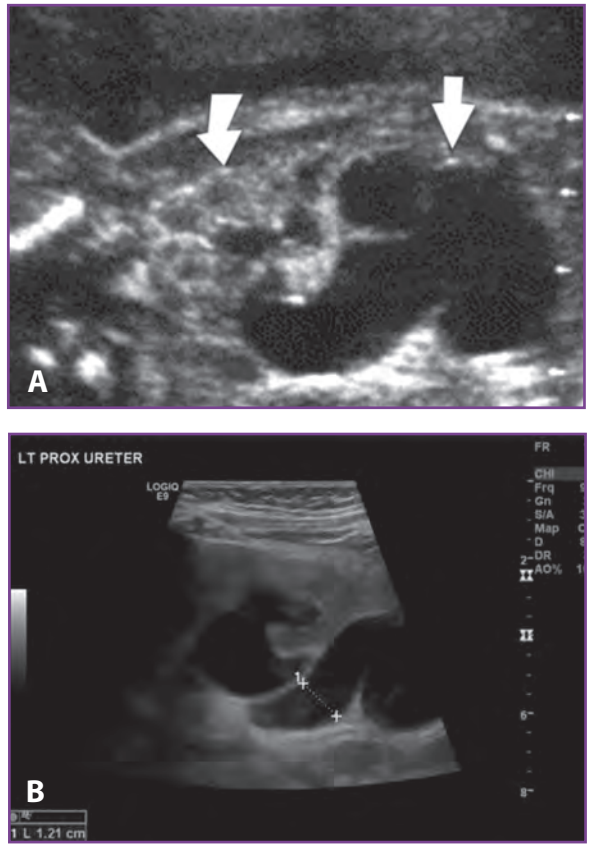


Figure 9-5. A, Prenatal ultrasonography (US) demonstrates a dilated kidney and ureter, also known as a *congenital megaureter.* **B,** Postnatal US shows a dilated ureter measuring 1.21 cm in diameter, behind the bladder.

incidence of approximately 1 in 1,500 to 1 in 2,000. Male patients are affected more than female patients, and the left side is more commonly affected than the right. UVJ is not associated with any specific congenital abnormalities.

Etiologic Origin

The etiologic origin of UVJ remains poorly defined in many children. However, there is often a lack of smooth muscle differentiation in the distal ureter that may create an obstruction.

Diagnosis and Evaluation

UVJ obstruction is most commonly detected during routine prenatal US. UTI is the most common symptomatic presentation, and severity can vary from simple UTI to pyelonephritis. Rarer presentations include intermittent loin or abdominal pain, abdominal swelling, or renal calculi.

All babies with a prenatal ureteral diameter of more than 7 mm should be investigated postnatally. Renal tract US is the first-line investigation to demonstrate ureteric dilatation and assess the severity of pelvicalyceal dilatation (**Figure 9-5B**). Voiding cystourethrography (VCUG) should be performed to exclude vesicoureteral reflux (VUR) as the cause for ureteral dilation. In boys and in cases of bilateral ureteric dilatation, this should be performed soon after birth to exclude bladder outlet obstruction from posterior urethral valves or strictures. Once VUR and bladder obstruction have been excluded, a MAG_3 diuretic renogram is obtained in babies with significant ureteric dilatation to look for obstruction at the UVJ and determine the differential renal function.

MAG_3 renogram drainage curves may be difficult to interpret in the presence of a grossly dilated ureter, as the isotope may be emptied from the kidney into the large ureter but not actually be draining into the bladder. Therefore, classifying a megaureter as obstructed or nonobstructed may require serial imaging over time. Similar to UPJ obstruction, features suggestive of UVJ obstruction in the asymptomatic patient include an initial differential renal function less than 40% or a decrease in function of 5% on serial scans and/or increasing dilatation at serial US. Delayed transit on the MAG_3 renogram in an asymptomatic patient in the presence of stable or improving dilatation and a differential renal function of greater than 40% is not consistent with obstruction.

Treatment Options and Outcomes

Conservative Management

Approximately 75% of dilated ureters detected prenatally will spontaneously resolve. Most patients are, therefore, managed conservatively by monitoring with US, initially every 3 to 6 months. Prophylactic antibiotics may be advisable for the first 6 to 12 months after birth to reduce the increased risk of UTIs in these patients. Breakthrough febrile UTIs may indicate a need for further intervention. Long-term follow-up with an occasional renal US examination is warranted, as symptoms may recur later in childhood or even in adulthood.

Surgical Management

Indications for surgery include differential function of less than 40%, especially when associated with massive hydroureteronephrosis or failure of conservative management, suggested by breakthrough febrile UTIs, pain, worsening dilatation, or deteriorating function.

Ureteric reimplantation is the surgical procedure of choice in children older than 1 year. The principle is to allow good drainage of the ureter without creating reflux. Postoperative follow-up is with a US and/or a nuclear renal scan to confirm correction of obstruction. In some cases, a longer period may be required before improvements are demonstrated, as the ureter may remain dilated for a prolonged period.

Ureteric reimplantation in a patient younger than 1 year is challenging because of the discrepancy between the dilated ureter and the small infantile bladder. Alternative strategies include temporary endoscopic stenting, cutaneous ureterostomy, or a refluxing ureteral reimplantation, whereby the dilated ureter is anastomosed to the bladder, bypassing the obstruction.

Vesicoureteral Reflux

The prevalence of VUR in children is estimated at 1% to 2% and accounts for 20% of infants with prenatally diagnosed UTD. By definition, VUR is when urine flows from the bladder back into the ureter and may go all the way back up into the kidney. Most cases of VUR

are asymptomatic and self-limiting, with approximately 50% resolution by the age of 18 months. However, VUR may be associated with UTIs, including pyelonephritis and renal scarring (also known as *reflux nephropathy*). The incidence is much higher (25%–40%) in those presenting with a febrile UTI. The diagnosis of VUR is 4 times more common in girls than in boys, and boys present predominantly when younger than 1 year, often with severely dilated upper tracts. Girls tend to present cumulatively throughout childhood after a UTI and with less upper tract dilatation.

Diagnosis and Evaluation

Investigation for VUR needs to be considered in infants with prenatally diagnosed UTD with ureteric dilatation. There is no correlation between US findings and the presence or extent of VUR, and the US findings may be within reference range even in the presence of high-grade VUR. VCUG is the standard-of-reference investigation and is indicated in cases of unilateral UTD with ureteric dilatation, bilateral UTD, dilated duplex systems with or without ureteroceles, or an abnormal bladder (**Figure 9-6**). VCUG enables grading of the VUR (see Chapter 8, Vesicoureteral Reflux) and demonstrates ureteral abnormalities (duplex or paraureteral diverticulum).

Treatment Options and Outcomes

Conservative Management

Many children with VUR do not require or benefit from intervention, which makes management controversial. This issue is covered further in Chapter 8, Vesicoureteral Reflux.

Surgical Management

The indications for surgical intervention may include development of febrile breakthrough UTI while taking appropriate antibiotic prophylaxis or after its discontinuation. Surgical intervention includes cystoscopic sub-ureteric injection of a bulking agent (eg, dextranomer–hyaluronic acid) or ureteral reimplantation.

Figure 9-6. Voiding cystourethrogram demonstrates bilateral, high-grade vesicoureteral reflux.

Multicystic Dysplastic Kidney

Multicystic dysplastic kidney (MCDK) is thought to result from failure of nephrogenic induction by the ureteric bud, which results in the formation of noncommunicating cysts, the absence of renal parenchyma, and a nonfunctioning cystic kidney (**Figure 9-7**).

It has an incidence of approximately 1 in 3,640 births and is most commonly unilateral. It is slightly more common in male patients (59%) and on the left side (53%). One-third of cases are associated with an abnormality in the contralateral kidney, including VUR in up to 20%, UPJ obstruction, or a ureterocele. Until recently, babies with a diagnosis of MCDK were routinely started on antibiotic prophylaxis until VUR was excluded; however, recent long-term studies suggest that the

VUR is commonly low grade (grades I–II, 74% of cases; grade III, 22% of cases), with only a slightly increased risk of UTI or renal scarring. Therefore, in the presence of a normal contralateral kidney at US, some physicians have questioned the utility of performing VCUG, as well as the need for antibiotic prophylaxis. Others consider the increased risk of VUR and any increased risk of pyelonephritis in the solitary functioning kidney to be justification for VCUG and use of prophylactic antibiotics in neonates who receive a diagnosis of MCDK.

Diagnosis and Evaluation

The natural history is routinely complete involution, especially if the MCDK length is 5 cm or shorter at first postnatal US (see **Figure 9-7**). One-third of cases involute by the second birthday; 47% involute at 5 years, and 59% at 10 years. ^{99m}Tc dimercaptosuccinic acid (DMSA) scanning is optional but has the benefit of confirming the diagnosis and ensuring that the contralateral kidney is normal and unscarred.

Treatment Options and Outcomes

Conservative Management

Initial management is conservative, with US follow-up performed to monitor involution of the MCDK and ensure good interval growth and hypertrophy of the contralateral kidney. The length of follow-up and

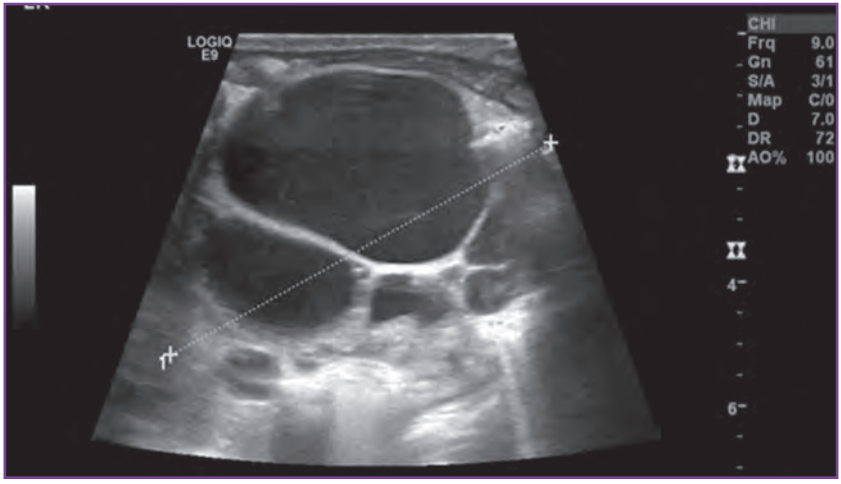


Figure 9-7. Postnatal ultrasonography demonstrates a multicystic dysplastic kidney.

indications for surgery have both diminished in recent years, due to evidence suggesting that risk of Wilms tumor or other kidney cancer, as well as the risk of hypertension, is no higher than in the general pediatric population.

Current guidelines advise monitoring of blood pressure, urine for proteinuria, and renal function in all children with a solitary kidney (MCDK or other etiologic origin), to identify those with markers of renal injury. Hypertension should be treated medically.

MCDK has been associated with genital anomalies—in particular, congenital absence of the vas deferens in men and uterus didelphys and obstructed hemivagina in women. The recommendation is for female patients with MCDK to undergo screening pelvic US after advanced puberty. There is no evidence of benefit for screening in male patients.

Surgical Management

A nephrectomy may also be considered where a large, palpable MCDK has failed to involute or enlarges (**Figure 9-8**). On rare occasions, an MCDK may be large enough to interfere with respiration or feeding, which is improved after nephrectomy. Another indication for nephrectomy includes failure of medical management of hypertension if the possibility exists that nephrectomy may cure the hypertension, if no other etiologic origins are identified.

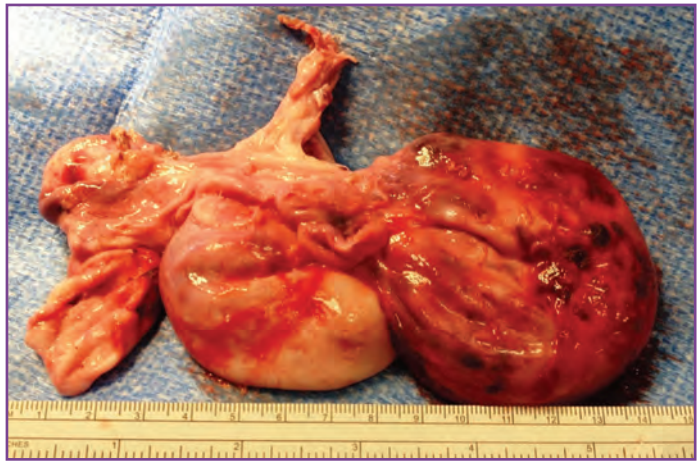


Figure 9-8. Nephrectomy specimen of a large, palpable multicystic dysplastic kidney that failed to involute spontaneously.

Duplex Systems and Ureterocele

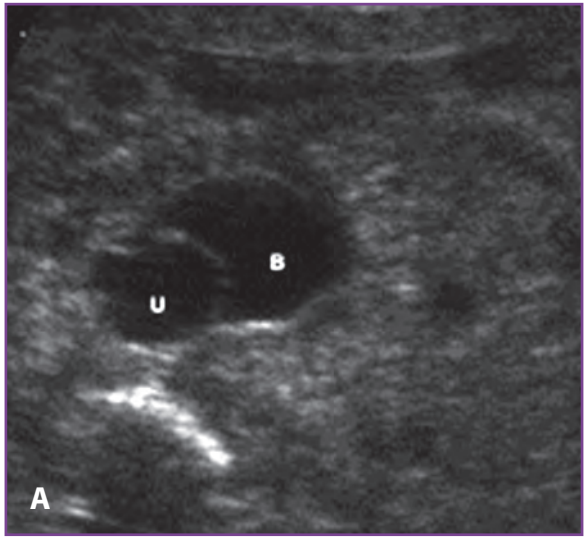
Duplication of the urinary tract has an incidence rate of 0.5% to 1.25% in postmortem series and is identified at prenatal US in 0.6% of pregnancies (**Figure 9-9A**).

Postnatal evaluation is only required if the duplex system is dilated or associated with a ureterocele. Duplex kidneys are seen approximately twice as frequently in female patients and are bilateral in one-fifth of cases. There appears to be a strong genetic predisposition: Up to 30% of patients have relatives with complete duplex kidneys, and up to 66% of relatives will have bifid systems, suggesting autosomal-dominant inheritance with variable expression and incomplete penetrance. Duplex kidneys form because of premature branching, or duplication, of the ureteric bud before it interacts with the metanephros to form the kidney. The upper pole of the kidney ureter may insert ectopically into the prostatic urethra, ejaculatory duct, seminal vesicle, vas deferens, or epididymis in boys or the urethra or vagina in girls. In boys, all these structures lie above the external urethral sphincter; therefore, the ectopic insertion does not cause incontinence. This is not the case in girls, where an ectopic ureter might appear with persistent dribbling incontinence at presentation.

Duplex systems may be associated with a cystic dilatation of the distal end of the upper moiety ureter as it inserts into the bladder, forming a cyst called a *ureterocele* (**Figure 9-9B**). Prenatally diagnosed UTD in a duplex system may be caused by obstruction (of the upper moiety, usually by a ureterocele or an ectopic insertion, or of the lower moiety, usually due to UPJ obstruction) or VUR (more commonly into the lower moiety, it but could affect both moieties).

Diagnosis and Evaluation

Postnatal renal tract US should be performed after 48 hours (if the UTD is unilateral) or more urgently if it is bilateral, as the ureterocele could cause bladder outlet obstruction (BOO), even if the baby appears to be voiding. Unilateral cases are subsequently investigated with VCUG to look for VUR and bladder emptying (**Figure 9-10**) and with renography to assess the split function of the upper and lower moieties (**Figure 9-11**). Upper moieties associated with an obstructing ureterocele or an ectopic ureter are often dysplastic and poorly functioning.



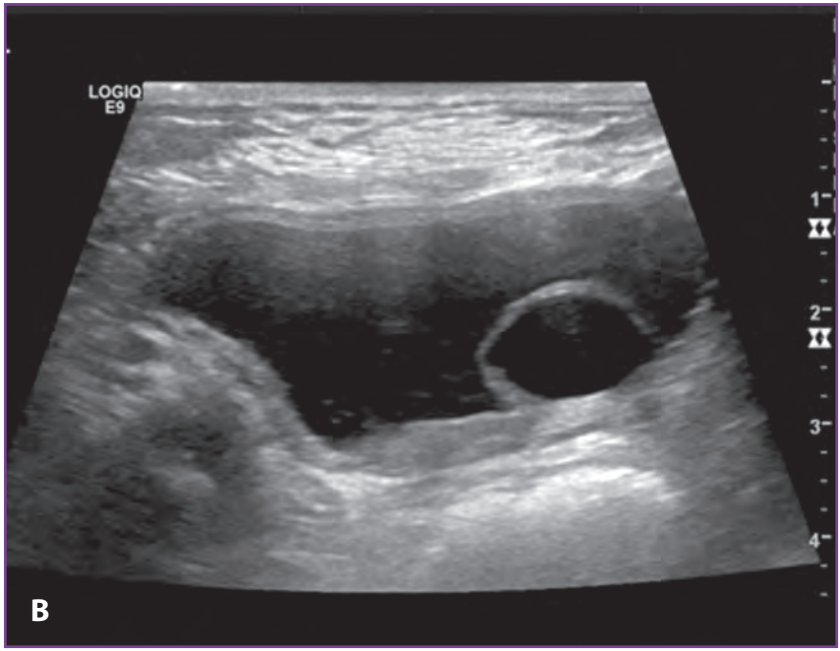


Figure 9-9. A, Prenatal ultrasonography (US) demonstrates a ureterocele (U) within the fetal bladder (B). **B,** Postnatal US shows the appearance of a ureterocele.

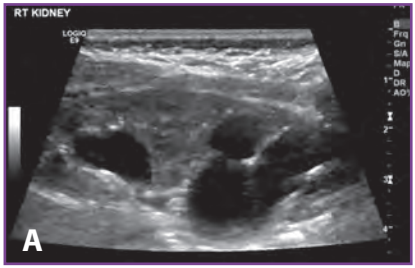


Figure 9-10. A, Ultrasonography shows a duplicated right kidney with dilation of the upper pole and lower pole renal pelvis. **B,** Voiding cystourethrography shows vesicoureteral reflux into both moieties of a right duplex system.

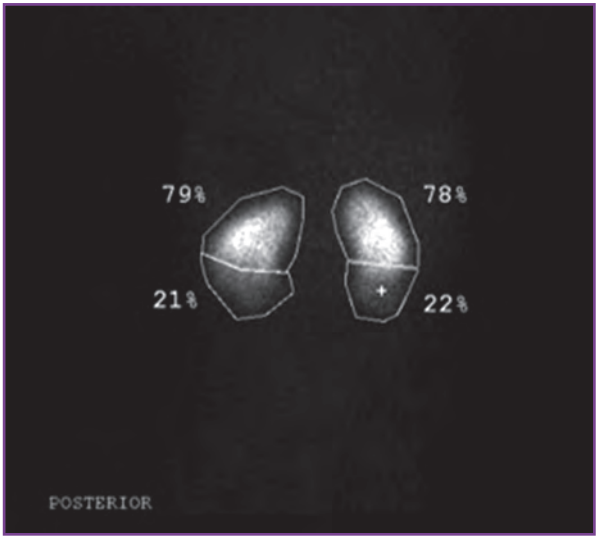


Figure 9-11. Renogram obtained with technetium 99m dimercaptosuccinic acid shows split function of bilateral duplex kidneys.

Treatment Options and Outcomes

All neonates with prenatal UTD in a duplex system should be started on prophylactic antibiotics. If there is suspicion for bladder outlet obstruction, the neonate requires catheterization and urgent evaluation with VCUG.

Further management will depend on the presence of symptoms, such as febrile UTIs or voiding difficulty and the function of the affected moiety. VUR in completely duplicated systems may initially be treated conservatively with observation and antibiotic prophylaxis, although the resolution rate is less than that for VUR in simplex systems (20% vs 50%, respectively, at 5-year follow-up).

Surgical intervention depends on the underlying cause for the UTD.

VUR in Duplex Systems

Surgical intervention for VUR is indicated after a breakthrough febrile UTI whilst on antibiotic prophylaxis. Endoscopic treatment is an acceptable first-line option, and there is no difference in the success rates of treatment of refluxing duplex and simplex systems with dextranomer–hyaluronic acid (64% vs 68%, respectively). Alternative surgical options for VUR in a duplex kidney include ureteric reimplantation into the bladder, a ureteroureterostomy connecting the refluxing ureter into the non-refluxing ureter, or a lower-moiety heminephroureterectomy if the refluxing moiety is nonfunctioning.

UPJ Obstruction in Duplex Systems

Lower-moiety UPJ obstruction, or UPJ obstruction in a partial duplex kidney, is an indication for pyeloplasty (**Figure 9-12**).

Ureterocele

Obstruction by a ureterocele may be initially treated endoscopically by puncturing the ureterocele, although this carries a risk of iatrogenic VUR. Failure of endoscopic management to relieve the obstruction may require a transurethral resection of the ureterocele. Alternatively, a more complex surgery may involve a heminephroureterectomy of the upper pole of the kidney, a ureteroureterostomy or excision of the ureterocele, and reimplantation. Small, asymptomatic, nonobstructive ureteroceles may not require any intervention.

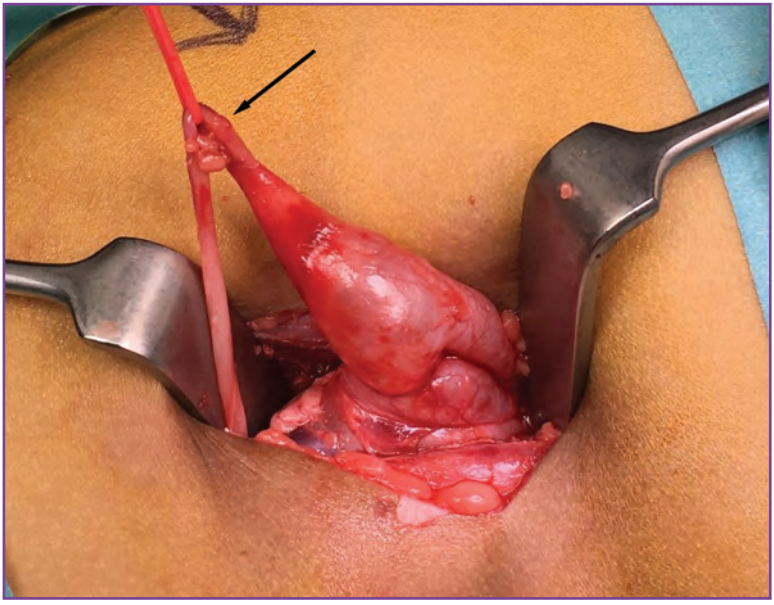


Figure 9-12. Intraoperative image of a ureteropelvic junction obstruction in a partial-duplex system.

Ectopic Ureter

"Cryptic duplex" kidneys in girls with dribbling incontinence may be notoriously difficult to identify and are not always apparent at US. Magnetic resonance urography may be helpful to clarify the anatomy and diagnose the ectopic ureter (**Figure 9-13**).

Ectopic ureters may be surgically managed with a ureteroureterostomy (the ectopic ureter is disconnected and anastomosed to the lower-moiety ureter), heminephroureterectomy of the nonfunctioning (often small) upper moiety, or reimplantation of the ectopic ureter into the bladder.

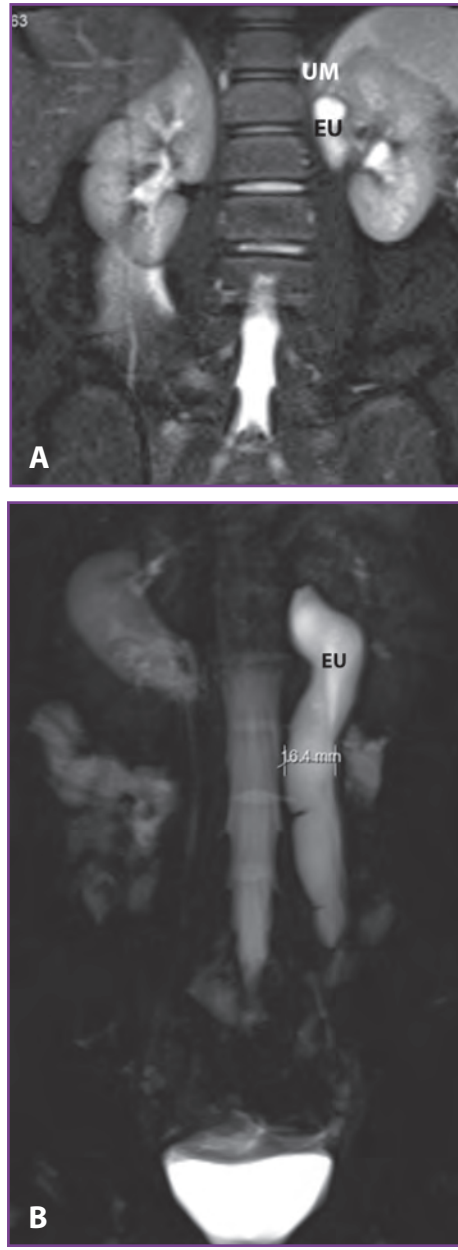


Figure 9-13. A, Coronal contrast-enhanced magnetic resonance images of a child with dribbling incontinence whose left ectopic ureter (EU) and cryptic dysplastic upper moiety (UM) were not evident at ultrasonography and technetium 99m dimercapto-succinic acid scanning. **B,** A 16.4-mm dilated left upper pole ectopic ureter is apparent.

Posterior Urethral Valves and Prune-belly Syndrome

When congenital UTD affects both kidneys, BOO, which may have serious consequences, needs to be excluded prior to discharging the baby home. Babies with BOO are often still able to void; hence, a wet diaper does not exclude obstruction. Several primary urethral disorders can cause congenital BOO, the most common being posterior urethral valves (PUVs) (**Figure 9-14**).

In PUV, which is a uniquely male condition, a "leaflet" or "membrane" spans the urethra, causing partial bladder outlet obstruction. A much rarer cause is urethral atresia, which causes complete obstruction by a membrane located at the distal end of the prostatic urethra. A third cause is prune-belly syndrome (PBS), whereby male infants are born with loose, wrinkled abdominal skin and poor abdominal musculature development, congenital UTD, and undescended testicles. Other rare causes of congenital BOO include prolapsed ureterocele, syringocoele

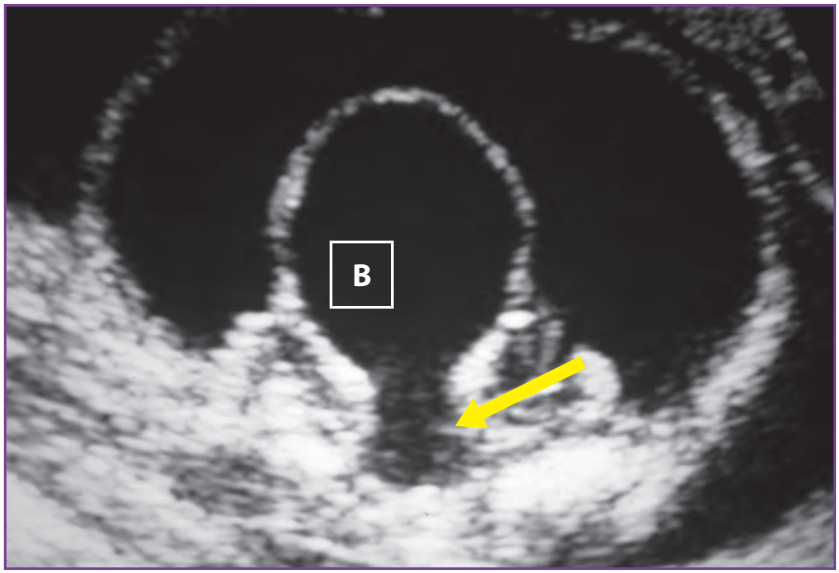


Figure 9-14. Prenatal ultrasonography demonstrates urinary bladder (B) dilatation and a "keyhole" sign, which represents the dilated posterior urethra (arrow) below the bladder and is suggestive of posterior urethral valves.

(dilatation of the duct of the Cowper gland, which could rupture and result in obstructive anterior urethral valves), and obstruction by hydrocolpos (fluid-filled uterus) in female patients who may have congenital urogenital anomalies. Finally, the megacystis microcolon syndrome, a generalized disorder of peristalsis with absent ganglion cells in the bladder wall, can manifest as congenital BOO.

Posterior Urethral Valves

PUV has an incidence of 1 in 8,000 male births. The embryological abnormality giving rise to PUV is unknown.

Diagnosis and Evaluation

All boys with bilateral prenatal UTD must be treated as if they are suspected of having BOO and PUV and should be managed as such until it has been excluded. Diagnosis is established via VCUG: In boys with PUV, the study usually shows an abnormal trabeculated bladder and a dilated posterior urethra (**Figure 9-15**). VUR is present in approximately 50% of cases (**Figure 9-16**).

PUV can also manifest postnatally in up to 40% of patients, with febrile UTI, poor urinary stream, or wetting. Renal US typically demonstrates a thin-walled bladder and bilateral UTD. However, the UTD may be unilateral in 15% of cases.

The presence of renal scarring and/or dysplasia is best assessed with DMSA renography when the infant is at least 2 months old.

Treatment Options and Outcomes

Initial Management

Early postnatal management involves respiratory support in babies with pulmonary hypoplasia, bladder catheterization, and stabilization of renal function. Postnatal US is usually performed around the second day after birth, followed by VCUG once the renal function is stable.

Renal Impairment

Effective postnatal management is extremely important, as early renal impairment is present in around one-quarter of patients, evidenced by increased plasma urea and/or creatinine levels. After initial treatment,

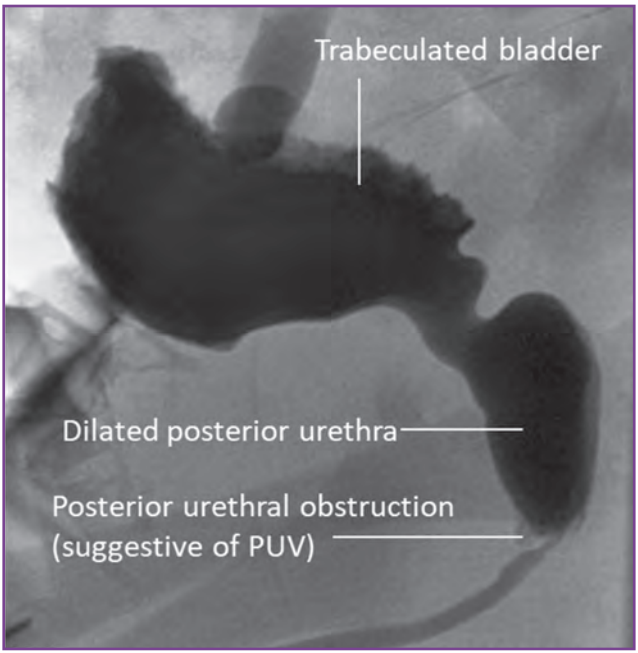


Figure 9-15. Voiding cystourethrography shows a trabeculated bladder and dilated posterior urethra, which are suggestive of posterior urethral valves (PUV).

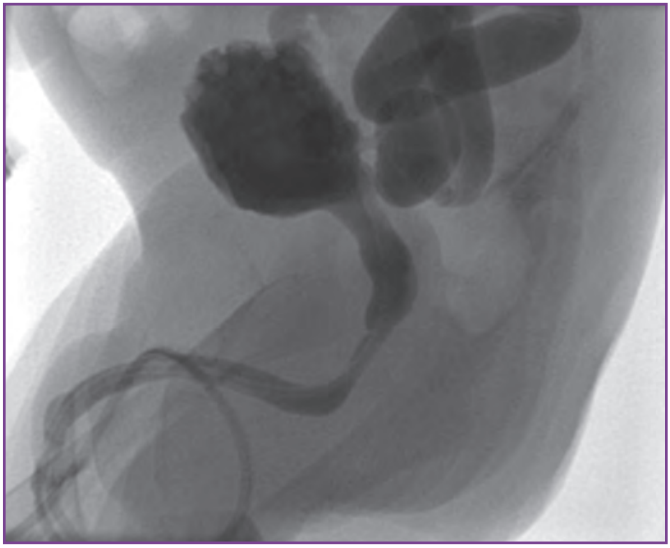


Figure 9-16. Bilateral high-grade vesicoureteral reflux and trabeculated bladder in a patient with posterior urethral valves.

renal function can improve in the first 3 years after birth, a phenomenon probably explained by the normal maturation in size and, thus, functional capacity of existing nephrons. Despite this early improvement, as childhood proceeds to early adulthood, between 30% and 70% of children with congenital BOO will experience a slow worsening of renal failure such that they require support with long-term dialysis and/or renal transplantation. Indeed, congenital BOO is the most common cause of end-stage renal failure requiring long-term dialysis and transplantation in boys; this risk of progression is greatest in those with high plasma creatinine levels (>1.0 mg/dL) after initial stabilization in the first year after birth. The most severe cases are also associated with pulmonary hypoplasia, a consequence of oligohydramnios and extensive UTD resulting in impaired lung development.

Surgical Management

Cystoscopy and endoscopic incision or resection of PUV with a pediatric resectoscope is possible in full-term babies. This, however, may be challenging in preterm neonates with a small urethra, and cutaneous vesicostomy (**Figure 9-17**) may be performed in these patients, with the valves resected at a later stage. After discharge, patients with PUV or BOO require long-term renal and bladder functional follow-up.

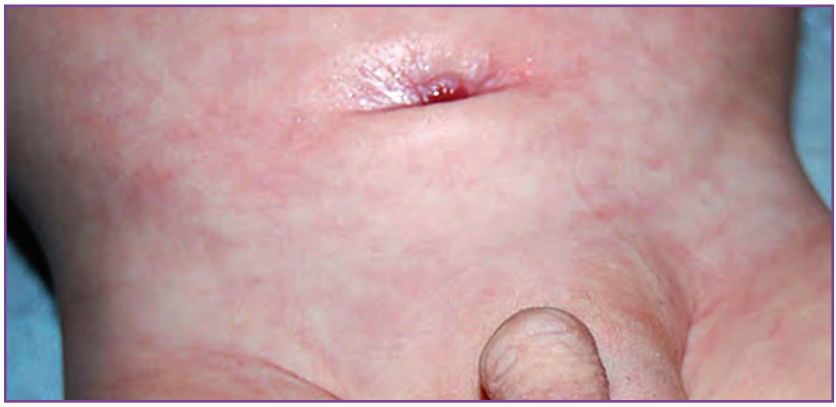


Figure 9-17. Vesicostomy in a patient with urethral atresia. From Vricella GJ, Coplen DE. Neonatal urogenital issues: evaluation and management. *NeoReviews*. 2017;18(6): e372–e385.

Outcomes

In spite of prenatal diagnosis and early renal and bladder care, renal deterioration to end-stage renal failure is still seen in a substantial number of patients. Bladder dysfunction necessitating clean intermittent catheterization and/or use of anticholinergics and nadir serum creatinine level of more than 1.0 mg/dL are associated with an increased risk of end-stage renal failure. Early gestational age at diagnosis (<24 weeks) and prenatal oligohydramnios or anhydramnios are also predictive of a poor renal outcome.

Bladder dynamics have an important role in maintaining renal integrity. Up to 50% of patients with PUV who have ongoing daytime incontinence at the age of 5 years have a significantly poorer renal outcome, highlighting the important role of bladder dysfunction. Boys with PUV have an overall 30% risk of developing chronic kidney disease, with 10% progressing to end-stage renal failure. Although bladder dysfunction may be initially managed medically by means of anticholinergics and clean intermittent catheterization, a number of patients require surgical management involving bladder augmentation (usually using a segment of ileum) and/or a catheterizable channel called a *Mitrofanoff*, whereby the appendix is used as a conduit between the bladder and the abdominal wall in patients who are unable or unwilling to catheterize urethrally.

Prune-belly (Triad) Syndrome

PBS, or triad syndrome, as described by Eagle and Barrett, is thought to be caused by an "abnormal angulation" of the urethra in a region where the prostate has incompletely developed, and this may in itself impair urine flow, rather than complete mechanical obstruction. This is associated with undescended testes and a "wrinkled" appearance of the abdominal wall, resembling a prune (**Figure 9-18**). A PBS phenotype may be seen in cases with urethral atresia, which may support the hypothesis that early BOO with massive bladder distention or ascites can result in atrophy of the abdominal wall musculature, induce renal dysplasia, and impair testicular descent. The appearance of urethral atresia has been described as a completely obstructed membrane below the verumontanum, with a hypoplastic distal urethra.

Figure 9-18. An infant with prune-belly syndrome and deficient abdominal musculature, resulting in hydroureters and hydronephrosis secondary to urethral obstruction. From Vricella GJ, Coplen DE. Neonatal urogenital issues: evaluation and management. *NeoReviews.* 2017;18(6):e372–e385.

Management

As the urinary tract pathophysiology of PBS is functional rather than mechanical, initial investigation relies on bladder-emptying assessment and urodynamic studies to evaluate bladder compliance and emptying. Most patients will require early initiation of clean intermittent catheterization or a vesicostomy (see **Figure 9-16**). Surgical management involves bilateral orchidopexies and plastic surgical "tightening" of the lax abdominal wall (abdominoplasty). Urinary tract reconstruction may be indicated at a later stage.

Outcome

Long-term outcome studies of boys with PBS report that up to 40% of patients may progress to chronic renal failure, with about one-half eventually requiring renal transplantation.

When to Refer

- A prenatal diagnosis of clinically significant UTD should be further investigated postnatally.
- Refer any child with clinically significant UTD (AP diameter >15 mm), worsening dilatation, or high-risk features at US.
- Refer all male neonates with bilateral UTD prenatally, where PUV is suspected.
- Refer any patient with a duplex system that is dilated at postnatal US or associated with a ureterocele.
- Refer all children with high-grade VUR who develop breakthrough UTIs while on antibiotic prophylaxis.
- Refer any child suspected of having UPJ obstruction.
- Refer any child in which there is ureteric dilatation of more than 7 mm, with or without associated UTD or suspected symptomatic UVJ obstruction.

Clinical Pearls

- High-risk features at prenatal US that show UTD include AP diameter larger than 15 mm, peripheral calyceal dilatation, ureteric dilatation or abnormality, bladder abnormality, and parenchymal abnormality.
- Prenatal bilateral UTD in male infants should be treated as PUV until it has been excluded.
- Babies with BOO are often still able to void; hence, a wet diaper does not exclude obstruction.
- BOO can manifest with unilateral UTD at presentation.
- In those with a dilated duplex system and a ureterocele, it is important to ensure good bladder emptying, as the ureterocele can cause BOO.
- Ongoing follow-up of children with scarred kidneys is essential, due to the potential long-term risk of hypertension, proteinuria, and renal impairment.

- Risk of hypertension is 10% with unilateral renal scarring and 20% with bilateral renal scarring.
- UTIs should be diagnosed when there is a febrile, culture-positive UTI. There is no indication for treatment in asymptomatic bacteriuria.

Resources for Parents

- National Kidney Federation. Posterior urethral values. http://www.kidney.org.uk/help-and-info/kids/kids-puv. Accessed July 16, 2018
- National Kidney Federation. MCDK. http://www.kidney.org.uk/help-and-info/kids/kids-mcdk. Accessed July 16, 2018
- InfoKID. Antenatal hydronephrosis: water on the kidneys. http://www.infokid.org.uk/antenatal-hydronephrosis. Accessed July 16, 2018
- InfoKID. Multicystic dysplastic kidney (MCDK): a congenital anomaly of the kidneys and urinary tract. http://www.infokid.org.uk/MCDK. Accessed July 16, 2018
- InfoKID. Posterior urethral valves (PUV). http://www.infokid.org.uk/PUV. Accessed July 16, 2018
- InfoKID. Vesicoureteral reflux (VUR) and reflux nephropathy. http://www.infokid.org.uk/VUR-and-reflux-nephropathy. Accessed July 16, 2018

Suggested Readings

Aslam M, Watson AR; Trent & Anglia MCDK Study Group. Unilateral multicystic dysplastic kidney: long term outcomes. *Arch Dis Child*. 2006;91(10):820–823

Farrugia MK. Fetal bladder outlet obstruction: embryopathology, in utero intervention and outcome. *J Pediatr Urol*. 2016;12(5):296–303

Farrugia MK, Hitchcock R, Radford A, Burki T, Robb A, Murphy F; British Association of Paediatric Urologists. British Association of Paediatric Urologists consensus statement on the management of the primary obstructive megaureter. *J Pediatr Urol*. 2014;10(1):26–33

Hoberman A, Greenfield SP, Mattoo TK, et al; RIVUR Trial Investigators. Antimicrobial prophylaxis for children with vesicoureteral reflux. *N Engl J Med*. 2014;370(25):2367–2376

Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). *J Pediatr Urol*. 2014;10(6):982–998

Nguyen HT, Herndon CDA, Cooper C, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. *J Pediatr Urol*. 2010;6(3):212–231

Peters CA, Skoog SJ, Arant BS Jr, et al. Summary of the AUA guideline on management of primary vesicoureteral reflux in children. *J Urol*. 2010;184(3):1134–1144

Psooy K; Collaboration with the Pediatric Urologists of Canada (PUC). Multicystic dysplastic kidney (MCDK) in the neonate: the role of the urologist. *Can Urol Assoc J*. 2016;10(1–2):18–24

Stein R, Dogan HS, Hoebeke P, et al; European Association of Urology; European Society for Pediatric Urology. Urinary tract infections in children: EAU/ESPU guidelines. *Eur Urol*. 2015;67(3):546–558

Tekgül S, Riedmiller H, Hoebeke P, et al; European Association of Urology. EAU guidelines on vesicoureteral reflux in children. *Eur Urol*. 2012;62(3):534–542

CHAPTER 10

Perinatal Urology

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Introduction

Prenatal urinary tract dilatation (UTD) is a common condition that occurs in 1% to 3% of all pregnancies. Prenatal identification of UTD includes a variety of possible etiologic origins and uropathies that affect the kidney, ureter, and/or bladder (**Table 10-1**).

Table 10-1. Etiologic Origins of Urinary Tract Dilatation Detected at Antenatal Ultrasonography

Etiologic Origin	Incidence Rate
Transient urinary tract dilation, physiological	50%–70%
Ureteropelvic junction obstruction	10%–30%
Vesicoureteral reflux	10%–40%
Ureterovesical junction obstruction, megaureter	5%–15%
Multicystic dysplastic kidney	2%–5%
Posterior urethral valves	1%–5%
Ureterocele, ectopic ureter, duplex system, urethral atresia, prune-belly syndrome, polycystic kidney disease	Uncommon

Adapted with permission from Nguyen HT, Herndon CD, Cooper C, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. *J Pediatr Urol.* 2010;6(3):212–231.

These conditions are discussed in detail in Chapter 9, Congenital Hydronephrosis. The aim of this chapter is to aid the primary care clinician in understanding the terminology used for grading UTD, development of risk stratification for prenatal and postnatal UTD, development of evaluation and management of postnatal UTD, and specific expectations for the more common diagnoses.

In most cases, UTD is transient or physiological and not clinically significant. In other cases, UTD in the fetus represents an obstructive condition or vesicoureteral reflux (VUR) that may have adverse effects on development and function and cause clinically significant morbidities. The goal is to separate benign UTD from clinically significant uropathy in the fetus, in an effort to minimize unnecessary testing in neonates and infants and detect cases of UTD that may require further perinatal evaluation (**Table 10-2**).

Defining and Classifying Urinary Tract Dilatation (UTD)

One of the more challenging aspects of managing cases of prenatal UTD is navigating the different grading systems used by providers. Different classifications systems have been developed to classify and grade prenatal and postnatal UTD. The scoring systems differ on the basis of the fetal ultrasonographic (US) criteria used. The different systems include the anteroposterior renal pelvic diameter (APRPD), the Society for Fetal Urology (SFU) grading system, and the more recent UTD classification system. The lack of uniformity in the definition and grading of UTD in part contributes to the inability to correctly correlate prenatal and postnatal US findings with the urological diagnosis.

Anteroposterior Renal Pelvic Diameter

APRPD (also known as *anterior-posterior diameter* or *APD*) is the measurement preferred by maternal-fetal medicine specialists to characterize the severity of renal pelvis dilatation. It is the maximum anterior-to-posterior diameter of the renal pelvis in the transverse plane and must be measured within the confines of the renal parenchyma (**Figure 10-1**).

Table 10-2. Urinary Tract Dilation Classification System Reference Range Values

Ultrasonographic Findings	Age at Presentation		
	Gestational Age 16–27 wk	Gestational Age ≥28 wk	Postnatally >48 h After Birth
Anteroposterior renal pelvis diameter	<4 mm	<7 mm	<10 mm
Calyceal dilation			
Central	No	No	No
Peripheral	No	No	No
Parenchymal thickness	Normal	Normal	Normal
Parenchymal appearance	Normal	Normal	Normal
Ureter(s)	Normal	Normal	Normal
Bladder	Normal	Normal	Normal
Unexplained oligohydramnios	No	No	NA

Abbreviation: NA, not applicable.

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Although APRPD measurement should be reliable, reproducible, and objective, it is unfortunately operator dependent for more clinically significant disease. Multiple investigators have evaluated renal pelvis size on the basis of gestational age to establish normative values. Several studies have demonstrated that the APRPD cutoffs are effective measures to predict both urological disease and the possible need for surgical intervention; however, there remains a lack of consistency across studies for various cutoff values, and there is no consensus on

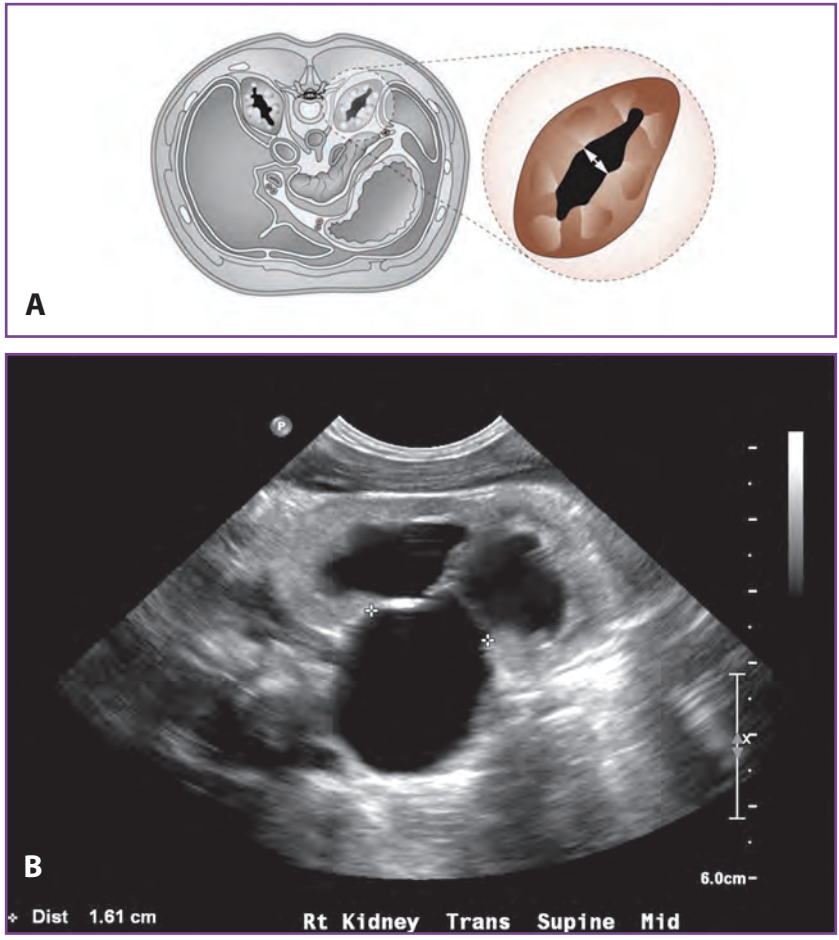

Figure 10-1. A, The anteroposterior renal pelvic diameter (APRPD), or anterior-posterior diameter, is the maximum anterior-to-posterior diameter of the renal pelvis measured in the transverse plane. The APRPD is frequently measured in the transverse plane at ultrasonography (US). **B.** Renal US demonstrates an APRPD of 1.61 cm.

A, Reprinted with permission from Timberlake MD, Herndon CD. Mild to moderate postnatal hydronephrosis—grading systems and management. *Nat Rev Urol*. 2013;10(11): 649–656.

the threshold APRPD that defines clinically significant prenatal UTD. Classically, APRPD larger than 4 mm during the second trimester and larger than 7 mm during the third trimester are the lowest cutoff values to diagnose potentially significant UTD in the fetus.

Society for Fetal Urology Grading System

The SFU classification system is the most widely used system for pediatric urologists and was developed to grade postnatal hydronephrosis. This subjective system is based on a 5-point system (grades 0–4) to grade UTD on the basis of the assessment of the degree of dilation of the collecting system, including the calyces, as well as the parenchymal integrity of the kidney (**Figure 10-2**).

Differentiating factors for grade 3 and 4 are based on the presence or absence of parenchymal thinning. This system is simple and has been found to be predictive of the need for surgical intervention, as well as preservation of renal function.

UTD Classification System

To promote uniformity and consistency for prenatal and postnatal grading of UTD, a system was developed that combined both objective and subjective parameters of the 2 previously described systems. Additionally, this system expanded the grading system to use findings not only within the kidney but in the lower urinary tract as well, by including the ureter and bladder. The system is based on 6 categories of US findings: *(a)* APRPD, *(b)* calyceal dilation, *(c)* renal parenchymal thickness, *(d)* renal parenchymal appearance, *(e)* bladder abnormalities, and *(f)* ureteral abnormalities.

In the UTD system, risk stratification is characterized by a classification system that consists of antenatal (A) and postnatal (P) risk assessment. Risk is categorized as follows: A1, low risk; A2, intermediate risk; and A3, high risk for antenatal UTD (**Figure 10-3**), and P1, low risk; P2, intermediate risk; and P3, high risk for postnatal UTD (**Figure 10-4**).

In the UTD grade A1 group, APRPD measuring 4 to 7 mm at less than 28 weeks' gestational age and 7 to less than 10 mm at more than 28 weeks' gestational age and the absence of calyceal involvement are considered low risk for postnatal urological pathologic findings. The UTD grade A2–A3 group is considered to be at increased risk for postnatal urological pathologic findings on the basis of APRPD larger than 7 mm at less than 28 weeks' gestational age and larger than 10 mm at more than 28 weeks' gestational age. The increased risk group is

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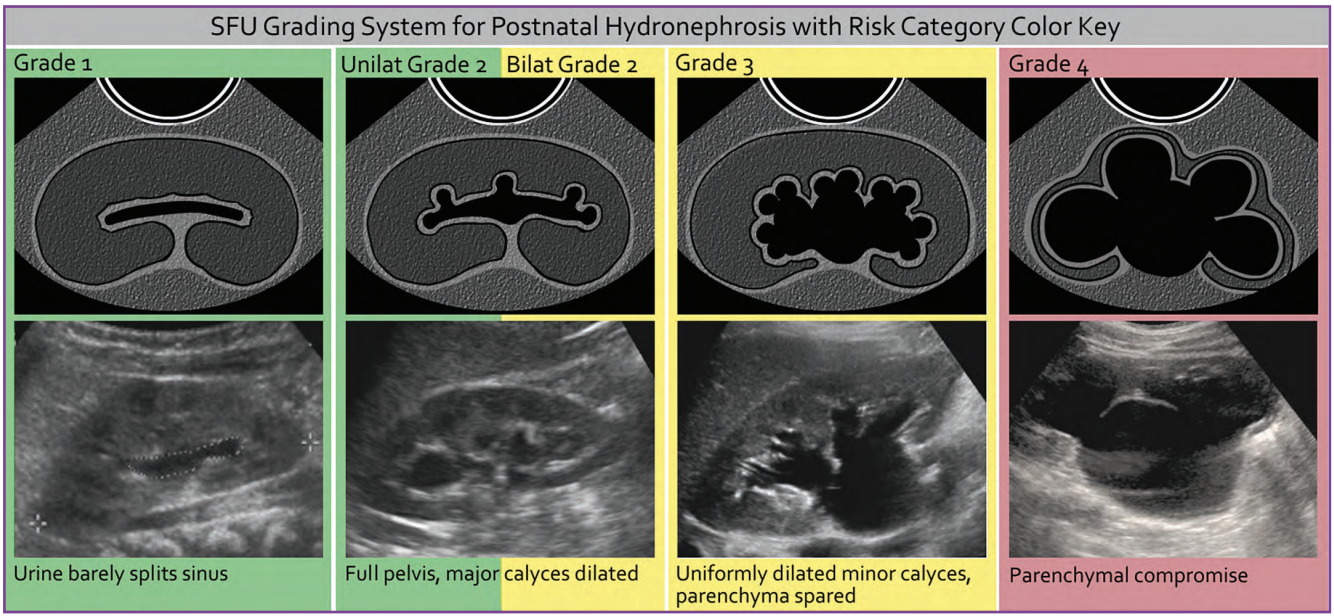

Figure 10-2. The Society for Fetal Urology grading system is based on renal ultrasonographic findings and uses a 5-point system (grades 0–4) to grade urinary tract dilation. The system is based on the degree of dilation of the collecting system and parenchymal integrity. Grade 0 is normal and not pictured. In grade 1, the urine splits the renal sinus. In grade 2, the urine fills the pelvis, and the major calyces are dilated. In grade 3, there are grade 2 findings plus dilation of the minor calyces and normal parenchyma. In grade 4, there are grade 3 findings, plus the parenchyma are thinned.

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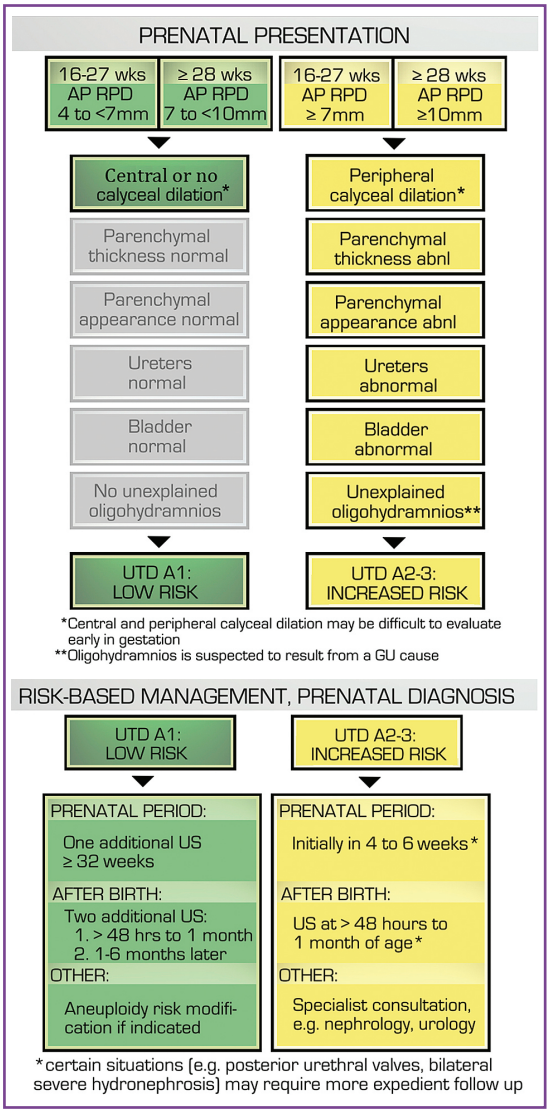

Figure 10-3. Urinary tract dilatation (UTD) prenatal risk stratification and risk-based management. Prenatal UTD grade A1 indicates low risk, and UTD grades A2 and A3 indicate increased risk. Stratification is based on the most concerning feature demonstrated at ultrasonography. AP, anteroposterior; GU, genitourinary; RPD, renal pelvic diameter; US, ultrasonography.

Adapted with permission from Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). *J Pediatr Urol.* 2014;10(6):982–998.

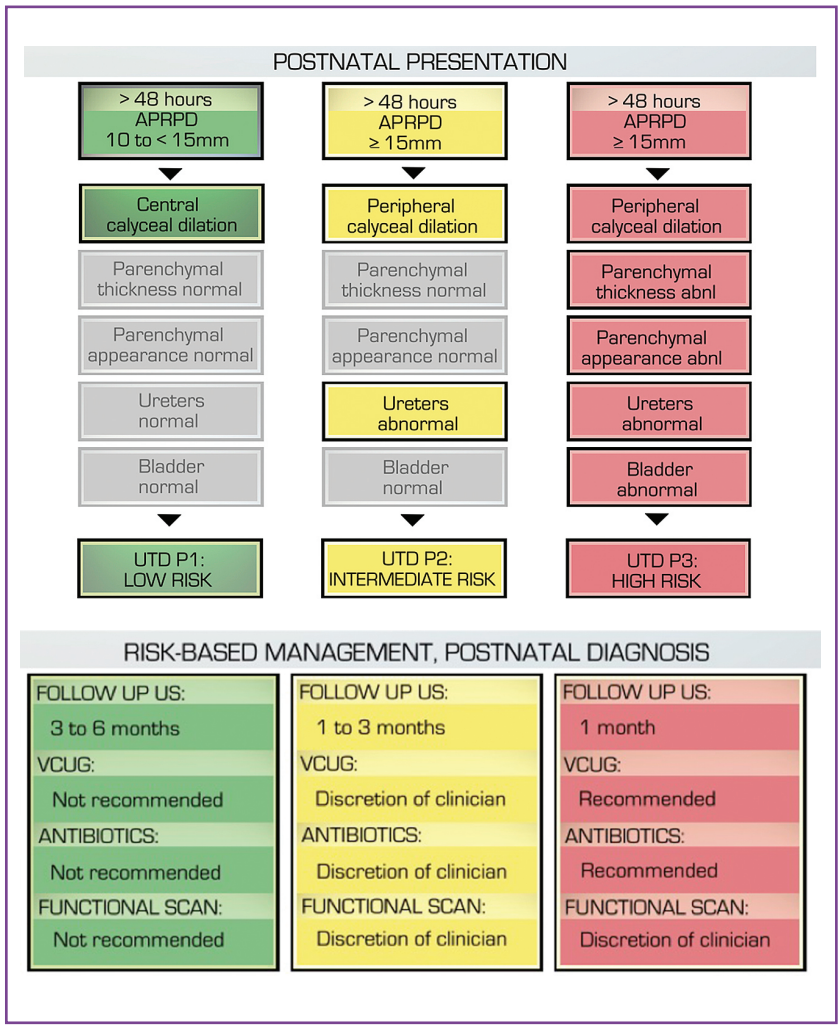

Figure 10-4. Urinary tract dilatation (UTD) postnatal risk stratification and risk-based management. Postnatal UTD grade P1 indicates low risk, UTD grade P2 indicates intermediate risk, and UTD grade P3 indicates high risk. Stratification is determined by the most concerning ultrasonographic finding. APRPD, anteroposterior renal pelvic diameter; US, ultrasonography; VCUG, voiding cystourethrography.

Adapted with permission from Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). *J Pediatr Urol.* 2014;10(6):982–998.

also associated with any of the following findings: peripheral calyceal dilation, abnormal parenchymal thickness or appearance, visibly dilated ureter, abnormal bladder, or the presence of unexplained oligohydramnios. Evaluation and management recommendations are based on the severity of risk.

Prenatal Magnetic Resonance Imaging

Magnetic resonance (MR) imaging does not use ionizing radiation and is a noninvasive procedure that is well tolerated in pregnancy and should be considered in cases in which US findings are indeterminate. MR imaging allows for in utero characterization of anatomic details of fetal genitourinary tract abnormalities and may provide additional information regarding different forms of urinary tract obstruction, ranging from ureteropelvic junction (UPJ) obstruction to posterior urethral valves. The reference standard for fetal imaging is US; however, the assessment may be limited by certain factors, such as amniotic fluid volume, fetal position, maternal body habitus, maternal bowel gas, or pelvic bony structures. The images provided by fetal MR imaging are high quality with detailed spatial resolution, and T2-weighted images provide excellent image contrast between fluid and solid tissue (**Figure 10-5**).

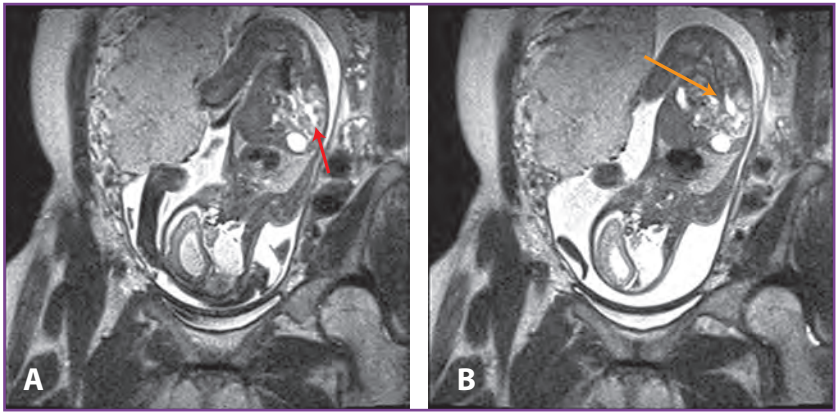

Figure 10-5. Fetal magnetic resonance images in a fetus of 25 weeks' gestational age show mild dilation of the renal pelvis of the left kidney. **A,** Arrow notes caliectasis of the left kidney. **B,** Arrow denotes fullness of the proximal left ureter.

Postnatal Management (Antibiotic Prophylaxis and Imaging)

The postnatal evaluation and management of prenatal UTD involves the use of renal US, the decision for recommendation of prophylactic antibiotics, the use of lower urinary tract imaging, and the use of renal scintigraphy (renal scanning).

Renal Ultrasonography

Ideally, the initial postnatal US should be delayed for at least 48 hours after birth to allow for resolution of initial postnatal oliguria, which may lead to underestimation of the degree of UTD. The degree of UTD may be compared to that identified on prenatal US images to classify the dilation as stable, improving, or worsening. Of note, up to 28% of patients have recurrence of UTD or present later with UPJ obstruction in the presence of a normal initial postnatal US finding. In addition, VUR can be present in up to 25% of neonates with an initially normal postnatal US finding. A normal postnatal renal US finding is demonstrated in **Figure 10-6**.

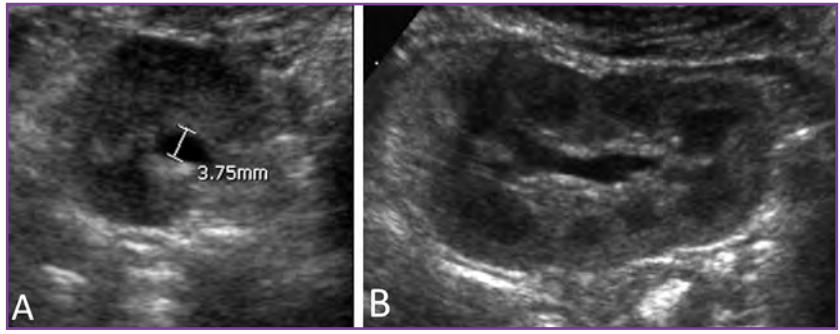

Figure 10-6. Normal postnatal ultrasonography (US) findings. **A,** US in the transverse plane exhibits an anteroposterior renal pelvic diameter of less than 10 mm, which is normal for age. **B,** US in the sagittal plane exhibits normal renal parenchyma without any dilation of the calyces. A normal bladder is not shown, and ureters are not seen.

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Voiding Cystourethrography

Voiding cystourethrography (VCUG) is performed to identify VUR or lower urinary tract obstruction. The decision to perform VCUG has undergone a paradigm shift over the past several decades and should be recommended on the basis of the patient risk of developing urological disease (eg, urinary tract infection [UTI]) as opposed to the historical need based on the likelihood of identifying VUR. The primary care physician should be acutely aware that many patients with low grades of UTD (UTD grade P1 and even P2) are no longer screened with VCUG but may have VUR in up to 20% of cases. Equally, the degree of prenatal UTD does not correlate well with the presence or severity of VUR. The timing of VCUG should be based on the severity of dilation. Most patients who undergo screening can be discharged, with subsequent imaging performed on an outpatient basis; however, in the male fetus with severe UTD, it may be advantageous to perform imaging after birth prior to discharge, to rule out urethral obstruction from posterior urethral valves. Prophylactic antibiotics should be used if patients are considered at high risk for UTI (UTD grade P2 or P3). Recently, a white paper on the standardization of VCUG technique was endorsed by the American Academy of Pediatrics, which serves to optimize the procedure and should allow for more consistent studies to be performed.

Renal Scintigraphy

In infants with persistent UTD, renal scintigraphy is used to identify surgical obstruction and evaluate differential renal function. Radionucleotide studies are inferior for demonstration of anatomic alterations when compared with other modalities, such as US, MR imaging, or computed tomography (an invasive test that requires intravenous hydration and a slight dose of radiation). The study involves administration of a diuretic and is measured in 2 phases: cortical imaging and tubular imaging. A technetium 99m mertiatide scan is best suited to evaluate kidney drainage as it is cleared by renal tubular secretion.

In infants with severe postnatal UTD, the major role of renal scintigraphy is to identify clinically relevant obstruction and differential renal function. The recent trends pertaining to prenatally detected UTD involve a more selective approach, with appropriately timed renal US studies and selective use of radionuclide scans in infants with persistent

postnatal UTD grade P2 or P3 (analogous to SFU grade 3 and 4 dilation) (**Figure 10-7**).

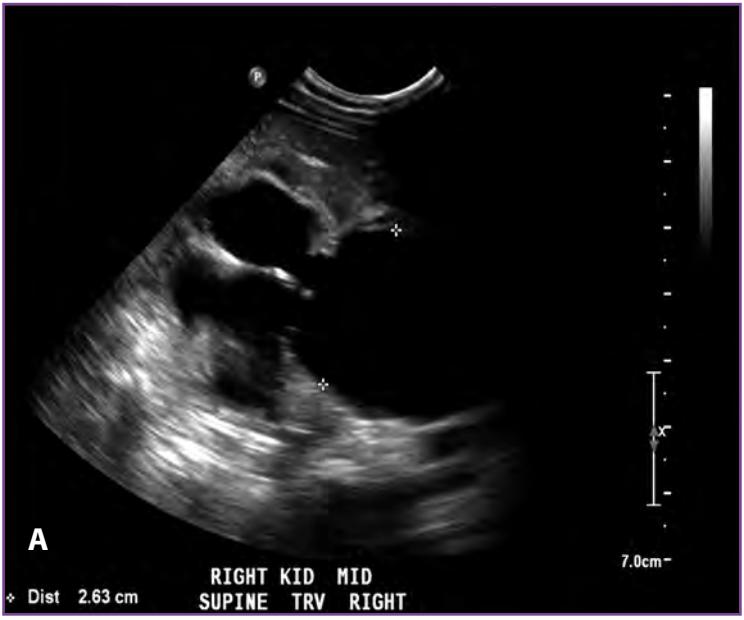
Magnetic Resonance Urography

MR urography is recognized as a valuable adjunct and is being more commonly used for the evaluation of UTD because it provides both morphologic and functional details. It provides further delineation of anatomic detail to localize the abnormality, differential function, and assessment of drainage. The cost, need for sedation, and use of gadolinium-based contrast material are some of the disadvantages that limit the widespread use of this modality (**Figure 10-8**).

Urinary Tract Infections and Prophylactic Antibiotics

The effectiveness of prophylactic antibiotics to prevent UTI for prenatal UTD has been challenged. A general consensus for factors that increase the risk of UTI include female sex, intact foreskin in male patients, and high-grade UTD (ie, SFU grades 3 and 4). Other areas identified in some studies but not validated in others that likely increase risk include ureteral dilation and VUR. In terms of VUR, it should be noted that a meaningful evidence-based risk assessment is not practical because of the lack of uniform screening for VUR.

Several studies have addressed the utility of prophylactic antibiotics or lack thereof to affect UTI. A systematic review of the literature showed support for prophylactic antibiotics preventing UTI in high-grade UTD but not low-grade UTD. The risk reduction was about 50%, with 14.6% developing UTI on prophylactic antibiotics and 28.9% developing UTI without the use of prophylactic antibiotics. However, other single-center studies have demonstrated conflicting results by demonstrating a lack of benefit, indifferent results, or a clear benefit for isolated grades that demonstrate postnatal VUR.



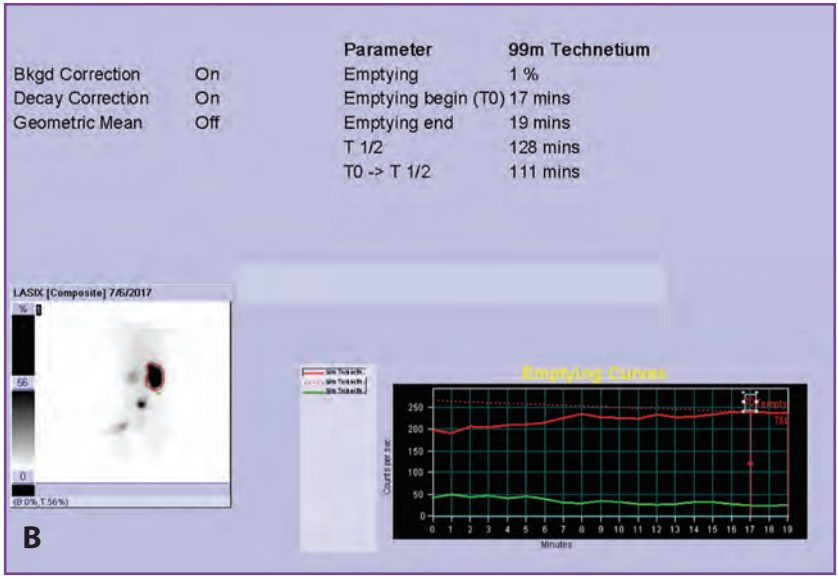


Figure 10-7. Renal scintigraphy. **A,** Ultrasonographic image shows a right kidney with dilation of the renal pelvis and calyces. **B,** Renal scintigraphy (images are posterior) demonstrates a dilated right kidney with retention of tracer when compared to the left kidney.

Figure 10-8. Coronal T2-weighted magnetic resonance urogram demonstrates bilateral urinary tract dilation in a 3-year-old girl. This single-shot fast spin-echo fat-saturated hydrogram shows severely dilated ureters (arrows) and collecting systems (*) and bilateral renal parenchymal thinning.

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Postnatal Evaluation Risk Stratification

The recommendation for prophylactic antibiotics and subsequent imaging is based on the postnatal classification (see **Figure 10-4**).

UTD Grade P1 (Low Risk)

Most patients seen postnatally will have UTD grade P1 (**Figure 10-9**), and recent data suggest that the use of prophylactic antibiotics is not beneficial because of the low risk of developing a UTI.

Furthermore, lower urinary tract imaging may not be performed, despite the fact that VUR may be present in up to 20% of this group—but this is also controversial. The primary care physician should be aware that

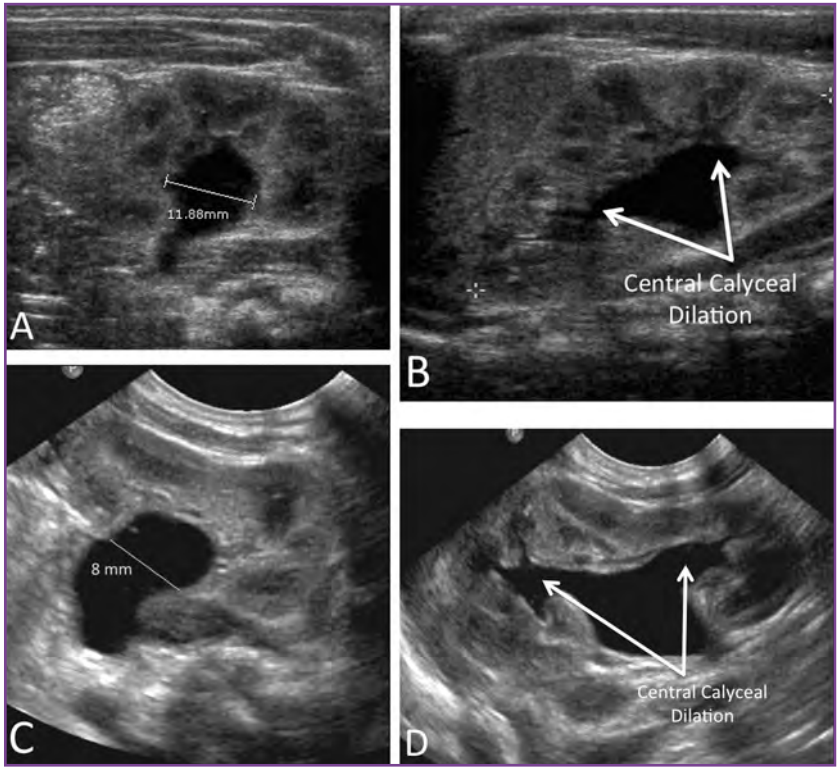

Figure 10-9. Urinary tract dilatation (UTD) grade P1 ultrasonographic (US) appearance. **A,** Transverse US exhibits an anteroposterior renal pelvic diameter (APRPD) of 10 to less than 15 mm. **B,** Sagittal US exhibits central but no peripheral calyceal dilation and normal renal parenchyma. The bladder (not shown) is normal, and the ureters are not seen. **C,** Transverse US exhibits APRPD less than 10 mm. **D,** Sagittal US demonstrates dilation of central calyces.

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this does not equate to the absence of VUR, especially when evaluating fever of unknown origin. Subsequent postnatal US is based on the probability of disease progression. Most patients with low-grade UTD rarely progress to higher grades and resolve within 48 months in almost all cases. Subsequent follow-up for these patients at low risk should range from 3 to 6 months after the initial postnatal US. In patients with a normal initial postnatal US finding obtained more than 48 hours after

birth, it is recommended that US be repeated within 3 to 6 months to ensure that resolution has occurred. Equally, when UTD resolves on further follow-up after initially being present postnatally, a second US examination is often performed at least 1 year later.

UTD Grade P2 (Intermediate Risk)

There is a lack of uniform agreement with respect to the use of prophylactic antibiotics, lower urinary tract imaging, or subsequent postnatal imaging for UTD grade P2 (**Figure 10-10**). The current recommendation

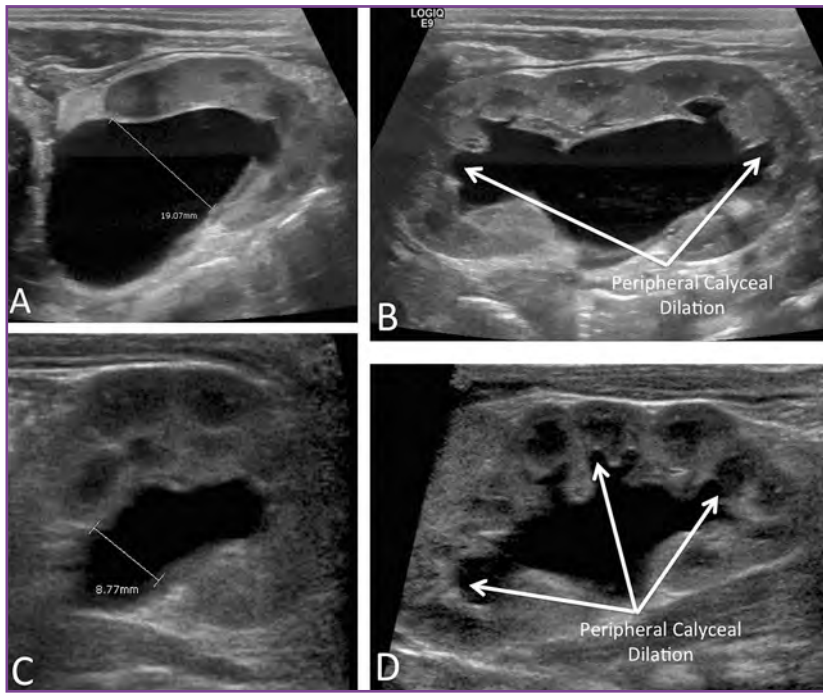

Figure 10-10. Urinary tract dilation (UTD) grade P2 ultrasonographic (US) appearance. **A,** Transverse US exhibits anteroposterior renal pelvic diameter (APRPD) of at least 15 mm. **B,** Sagittal US exhibits dilation of the peripheral calyces, with normal renal parenchymal thickness and appearance. There are no bladder abnormalities (not shown). This is a second example of UTD grade P2 postnatal US findings. **C,** Transverse US exhibits an APRPD of less than 10 mm. **D,** Sagittal US exhibits dilation of both peripheral and central calyces.

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for prophylactic antibiotics, VCUG, and renal scintigraphy is left to the discretion of the physician, and a clear need for further research exists for this population.

UTD Grade P3 (High Risk)

The use of initial prophylactic antibiotics is recommended for UTD grade P3 (**Figure 10-11**).

The use of lower urinary tract imaging and renal scintigraphy is also highly recommended for UTD grade P3. The current recommendation is to perform renal US at 4- to 6-week intervals postnatally to assess the patient for disease progression. This study can be combined with VCUG if not performed prior to discharge. Renal scintigraphy can be performed at subsequent visits but generally should be conducted more than 4 weeks after birth and before 3 months of age.

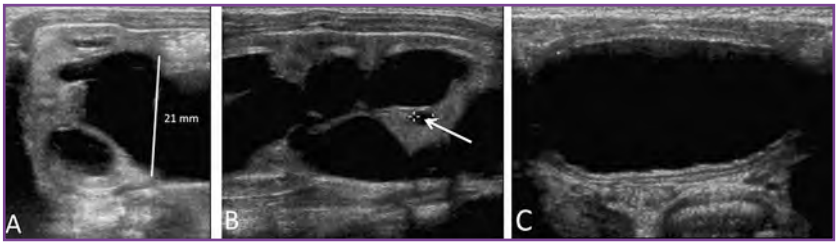

Figure 10-11. Urinary tract dilation grade P3 ultrasonographic (US) appearance. **A,** Transverse US exhibits anteroposterior renal pelvic diameter of at least 15 mm, with peripheral dilation of the calyces. **B,** Sagittal US exhibits parenchymal thinning and cysts (arrow). **C,** Bladder US demonstrates increased wall thickness.

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Summary

In summary, UTD is the most common congenital anomaly detected prenatally. Advances in imaging have increased the detection and characterization of prenatal and postnatal genitourinary abnormalities such as UTD; however, further investigation is needed to determine which are clinically significant and will require some form of intervention. Recently, a new classification system (the UTD system) has been

developed that aligns the historically different grading systems used prenatally and postnatally. This serves to allow for the development of a risk-stratification system in addition to allowing for a platform for more meaningful research. Most patients demonstrate low-risk (UTD grade P1) disease and do not need prophylactic antibiotics or lower urinary tract imaging, while most patients with high-risk (UTD grade P3) disease will benefit from these interventions. Although patients with intermediate-risk (UTD grade P2) disease may have increased risk of UTI, a lack of consensus exists with respect to the need for prophylactic antibiotics and lower urinary tract imaging, which warrants further research.

When to Refer

The primary care physician should be aware that the recommendations given herein apply to isolated, unilateral UTD. The following are indications for referral:

- Infants with persistent UTD (APRPD >10 mm) should be referred to a center with pediatric urology and/or pediatric nephrology services. These patients will require counseling and an informed, shared decision-making process that includes the risks of UTI, the benefits of prophylactic antibiotics, and the utility of other invasive testing, such as VCUG and renal scintigraphy.
- In situations in which UTD is bilateral, concerns for bladder outlet obstruction exist, or multiorgan disease is present, expert consultation by a pediatric urologist and/or pediatric nephrologist is recommended.
- The presence of other findings, such as multiorgan disease with extrarenal anomalies, gestational age, and abnormal amniotic fluid volume, should also be factored in when considering a referral to a pediatric urology, nephrology, and maternal-fetal medicine team.

Clinical Pearls

- Prenatal UTD is a common condition that occurs in 1% to 3% of all pregnancies. The goal is to separate benign UTD from clinically significant uropathy in the fetus or neonate, in an effort to minimize unnecessary testing.

- In most instances, UTD is transient or not clinically significant; however, VUR and obstructive uropathies are important causes of UTD that should be diagnosed after birth because of potential adverse effects.
- The primary care clinician should have an understanding of the UTD grading system terminology, to aid in risk stratification and to guide shared decision-making.
- Different classification systems exist to grade and classify prenatal and postnatal UTD. The different systems include the APRPD, the SFU grading system, and the UTD classification system.
- Factors that increase the risk of UTI include female sex, intact foreskin in male patients, and high-grade UTD (ie, SFU grades 3 and 4) and ureteral dilation.
- Patients with UTD grade P1 are at low risk, and follow-up imaging should occur 3 to 6 months after original postnatal US examination.
- UTD grade P2 represents patients with intermediate risk. There is a lack of general consensus with respect to antibiotics and lower urinary tract imaging. The need for antibiotics, VCUG, and functional scans is at the discretion of the clinician.
- Patients with UTD grade P3 are high risk; thus, initial antibiotic prophylaxis is recommended. It is also recommended that US be repeated every 4 to 6 weeks to assess the patient for disease progression. VCUG is recommended in the evaluation; however, functional scans are at the discretion of the clinician.

Suggested Readings

Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). *J Pediatr Urol*. 2014;10(6):982–998. http://www.jpurol.com/article/S1477-5131(14)00310-6/fulltext. Accessed October 17, 2018

Lee RS, Cendron M, Kinnamon DD, Nguyen HT. Antenatal hydronephrosis as a predictor of postnatal outcome: a meta-analysis. *Pediatrics*. 2006;118(2):586–593

Nguyen HT, Herndon CDA, Cooper C, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. *J Pediatr Urol*. 2010;6(3):212–231

Braga LH, Farrokhyar F, D'Cruz J, Pemberton J, Lorenzo AJ. Risk factors for febrile urinary tract infection in children with prenatal hydronephrosis: a prospective study. *J Urol*. 2015;193(5 Suppl):1766–1771

Braga LH, McGrath M, Farrokhyar F, Jegatheeswaran K, Lorenzo AJ. Associations of initial Society for Fetal Urology grades and urinary tract dilatation risk groups with clinical outcomes in patients with isolated prenatal hydronephrosis. *J Urol*. 2017;197 (3 Pt 2):831–837

Jackson J, Zee R, Corbett S, Herndon CA. A practice pattern assessment of members of Society of Pediatric Urology for the evaluation and treatment of urinary tract dilation. Societies for Pediatric Urology Web site. http://spuonline.org/abstracts/2016/MP13.cgi. Accessed October 17, 2018

References

1. Hamilton BE, Martin JA, Ventura SJ. Births: preliminary data for 2012. *Natl Vital Stat Rep*. 2013;62(3):1–20
2. Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). *J Pediatr Urol*. 2014;10(6):982–998
3. Zanetta VC, Rosman BM, Bromley B, et al. Variations in management of mild prenatal hydronephrosis among maternal-fetal medicine obstetricians, and pediatric urologists and radiologists. *J Urol*. 2012;188(5):1935–1939
4. Odibo AO, Marchiano D, Quinones JN, Riesch D, Egan JF, Macones GA. Mild pyelectasis: evaluating the relationship between gestational age and renal pelvic anterior-posterior diameter. *Prenat Diagn*. 2003;23(10):824–827
5. Chitty LS, Altman DG. Charts of fetal size: kidney and renal pelvis measurements. *Prenat Diagn*. 2003;23(11):891–897
6. Dhillon HK. Prenatally diagnosed hydronephrosis: the Great Ormond Street experience. *Br J Urol*. 1998;81(Suppl 2):39–44
7. Coplen DE, Austin PF, Yan Y, Blanco VM, Dicke JM. The magnitude of fetal renal pelvic dilatation can identify obstructive postnatal hydronephrosis, and direct postnatal evaluation and management. *J Urol*. 2006;176(2):724–727, discussion 727
8. Shamshirsaz AA, Ravangard SF, Egan JF, et al. Fetal hydronephrosis as a predictor of neonatal urologic outcomes. *J Ultrasound Med*. 2012;31(6):947–954
9. Fernbach SK, Maizels M, Conway JJ. Ultrasound grading of hydronephrosis: introduction to the system used by the Society for Fetal Urology. *Pediatr Radiol*. 1993;23(6):478–480
10. Erickson BA, Maizels M, Shore RM, et al. Newborn society of fetal urology grade 3 hydronephrosis is equivalent to preserved percentage differential function. *J Pediatr Urol*. 2007;3(5):382–386

11. Marks A, Maizels M, Mickelson J, et al. Effectiveness of the computer enhanced visual learning method in teaching the society for fetal urology hydronephrosis grading system for urology trainees. *J Pediatr Urol*. 2011;7(2):113–117

12. Siddique J, Lauderdale DS, VanderWeele TJ, Lantos JD. Trends in prenatal ultrasound use in the United States: 1995 to 2006. *Med Care*. 2009;47(11):1129–1135

13. Lee RS, Cendron M, Kinnamon DD, Nguyen HT. Antenatal hydronephrosis as a predictor of postnatal outcome: a meta-analysis. *Pediatrics*. 2006;118(2):586–593

14. Hayashi S, Sago H, Kashima K, et al. Prenatal diagnosis of fetal hydrometrocolpos secondary to a cloacal anomaly by magnetic resonance imaging. *Ultrasound Obstet Gynecol*. 2005;26(5):577–579

15. Huisman TA, van der Hoef M, Willi UV, Gobet R, Lebowitz RL. Pre- and postnatal imaging of a girl with a cloacal variant. *Pediatr Radiol*. 2006;36(9):991–996

16. Warne S, Chitty LS, Wilcox DT. Prenatal diagnosis of cloacal anomalies. *BJU Int*. 2002; 89(1):78–81

17. Kajbafzadeh AM, Payabvash S, Sadeghi Z, et al. Comparison of magnetic resonance urography with ultrasound studies in detection of fetal urogenital anomalies. *J Pediatr Urol*. 2008;4(1):32–39

18. Dejter SW, Gibbons MD. The fate of infant kidneys with fetal hydronephrosis but initially normal postnatal sonography. *J Urol*. 1989;142(2 Pt 2):661–662, discussion 667–668

19. Laing FC, Burke VD, Wing VW, Jeffrey RB Jr, Hashimoto B. Postpartum evaluation of fetal hydronephrosis: optimal timing for follow-up sonography. *Radiology*. 1984;152(2):423–424

20. Herndon CD. Editorial comment. *J Urol*. 2015;193(2):642

21. Herndon CD, McKenna PH, Kolon TF, Gonzales ET, Baker LA, Docimo SG. A multicenter outcomes analysis of patients with neonatal reflux presenting with prenatal hydronephrosis. *J Urol*. 1999;162(3 Pt 2):1203–1208

22. Aksu N, Yavaşcan O, Kangin M, et al. Postnatal management of infants with antenatally detected hydronephrosis. *Pediatr Nephrol*. 2005;20(9):1253–1259

23. Gatti JM, Broecker BH, Scherz HC, Perez-Brayfield MR, Kirsch AJ. Antenatal hydronephrosis with postnatal resolution: how long are postnatal studies warranted? *Urology*. 2001;57(6):1178

24. Zee RS, Herndon CDA. Prenatal diagnosis of congenital anomalies of the kidney and urinary tract. In: *Congenital Anomalies of the Kidney and Urinary Tract*. Basel, Switzerland: Springer International Publishing; 2016:265–286

25. Phan V, Traubici J, Hershenfield B, Stephens D, Rosenblum ND, Geary DF. Vesicoureteral reflux in infants with isolated antenatal hydronephrosis. *Pediatr Nephrol*. 2003;18(12):1224–1228

26. Frimberger D, Mercado-Deane MG; American Academy of Pediatrics Section on Urology, Section on Radiology. Establishing a standard protocol for the voiding cystourethrography. *Pediatrics*. 2016;138(5):e20162590

27. Conway JJ, Maizels M. The "well tempered" diuretic renogram: a standard method to examine the asymptomatic neonate with hydronephrosis or hydroureteronephrosis. A report from combined meetings of The Society for Fetal Urology and members of The Pediatric Nuclear Medicine Council–The Society of Nuclear Medicine. *J Nucl Med*. 1992;33(11):2047–2051

28. Nguyen HT, Herndon CD, Cooper C, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. *J Pediatr Urol*. 2010;6(3):212–231

29. Jones RA, Perez-Brayfield MR, Kirsch AJ, Grattan-Smith JD. Renal transit time with MR urography in children. *Radiology*. 2004;233(1):41–50

30. McMann LP, Kirsch AJ, Scherz HC, et al. Magnetic resonance urography in the evaluation of prenatally diagnosed hydronephrosis and renal dysgenesis. *J Urol*. 2006;176 (4 Pt 2):1786–1792

31. Perez-Brayfield MR, Kirsch AJ, Jones RA, Grattan-Smith JD. A prospective study comparing ultrasound, nuclear scintigraphy and dynamic contrast enhanced magnetic resonance imaging in the evaluation of hydronephrosis. *J Urol*. 2003;170 (4 Pt 1):1330–1334

32. Braga LH, Mijovic H, Farrokhyar F, Pemberton J, DeMaria J, Lorenzo AJ. Antibiotic prophylaxis for urinary tract infections in antenatal hydronephrosis. *Pediatrics*. 2013;131(1):e251–e261

33. Braga LH, Farrokhyar F, D'Cruz J, Pemberton J, Lorenzo AJ. Risk factors for febrile urinary tract infection in children with prenatal hydronephrosis: a prospective study. *J Urol*. 2015;193(5 Suppl):1766–1771

34. Zee RS, Herbst KW, Kim C, et al. Urinary tract infections in children with prenatal hydronephrosis: a risk assessment from the Society for Fetal Urology Hydronephrosis Registry. *J Pediatr Urol*. 2016;12(4):261.e1–261.e7

35. Merguerian PA, Herz D, McQuiston L, Van Bibber M. Variation among pediatric urologists and across 2 continents in antibiotic prophylaxis and evaluation for prenatally detected hydronephrosis: a survey of American and European pediatric urologists. *J Urol*. 2010;184(4 Suppl):1710–1715

36. Braga LH, Pemberton J, Heaman J, DeMaria J, Lorenzo AJ. Pilot randomized, placebo controlled trial to investigate the effect of antibiotic prophylaxis on the rate of urinary tract infection in infants with prenatal hydronephrosis. *J Urol*. 2014;191(5 Suppl):1501–1507

37. Coelho GM, Bouzada MC, Pereira AK, et al. Outcome of isolated antenatal hydronephrosis: a prospective cohort study. *Pediatr Nephrol*. 2007;22(10):1727–1734

38. Alconcher L, Tombesi M. Mild antenatal hydronephrosis: management controversies. *Pediatr Nephrol*. 2004;19(7):819–820

39. Estrada CR, Peters CA, Retik AB, Nguyen HT. Vesicoureteral reflux and urinary tract infection in children with a history of prenatal hydronephrosis—should voiding cystourethrography be performed in cases of postnatally persistent grade II hydronephrosis? *J Urol*. 2009;181(2):801–806, discussion 806–807

40. Ismaili K, Avni FE, Hall M; Brussels Free University Perinatal Nephrology (BFUPN) Study Group. Results of systematic voiding cystourethrography in infants with antenatally diagnosed renal pelvis dilation. *J Pediatr*. 2002;141(1):21–24

41. Zee RS, Herndon CDA, Cooper CS, et al. Time to resolution: a prospective evaluation from the Society for Fetal Urology hydronephrosis registry. *J Pediatr Urol*. 2017;13(3):316.e1–316.e5

42. Jackson J, Zee R, Corbett S, Herndon CA. A practice pattern assessment of members of Society of Pediatric Urology for the evaluation and treatment of urinary tract dilation. Societies for Pediatric Urology Web site. http://spuonline.org/abstracts/2016/MP13.cgi. Accessed October 17, 2018

43. Herndon CD. Fetal urology. *J Pediatr Urol*. 2012;8(2):120

44. Mandell J, Kinard HW, Mittelstaedt CA, Seeds JW. Prenatal diagnosis of unilateral hydronephrosis with early postnatal reconstruction. *J Urol*. 1984;132(2):303–307

45. Maayan-Metzger A, Lotan D, Jacobson JM, et al. The yield of early postnatal ultrasound scan in neonates with documented antenatal hydronephrosis. *Am J Perinatol*. 2011;28(8):613–618

46. Barbosa JA, Chow JS, Benson CB, et al. Postnatal longitudinal evaluation of children diagnosed with prenatal hydronephrosis: insights in natural history and referral pattern. *Prenat Diagn*. 2012;32(13):1242–1249

47. Herndon CD, DeCambre M, McKenna PH. Changing concepts concerning the management of vesicoureteral reflux. *J Urol*. 2001;166(4):1439–1443

48. Ross SS, Kardos S, Krill A, et al. Observation of infants with SFU grades 3-4 hydronephrosis: worsening drainage with serial diuresis renography indicates surgical intervention and helps prevent loss of renal function. *J Pediatr Urol*. 2011;7(3):266–271

49. Braga LH, McGrath M, Farrokhyar F, Jegatheeswaran K, Lorenzo AJ. Associations of initial Society for Fetal Urology grades and urinary tract dilatation risk groups with clinical outcomes in patients with isolated prenatal hydronephrosis. *J Urol*. 2017;197(3 Pt 2):831–837

50. Cain MP, Rink RC, Thomas AC, Austin PF, Kaefer M, Casale AJ. Symptomatic ureteropelvic junction obstruction in children in the era of prenatal sonography—is there a higher incidence of crossing vessels? *Urology*. 2001;57(2):338–341

51. Sweeney DD, Ost MC, Schneck FX, Docimo SG. Laparoscopic pyeloplasty for ureteropelvic junction obstruction in children. *J Laparoendosc Adv Surg Tech A*. 2011;21(3):261–265

52. Minnillo BJ, Cruz JA, Sayao RH, et al. Long-term experience and outcomes of robotic assisted laparoscopic pyeloplasty in children and young adults. *J Urol*. 2011;185(4):1455–1460

53. Herndon CD, Herbst K, Smith C. The transition from open to laparoscopic pediatric pyeloplasty: a single-surgeon experience. *J Pediatr Urol*. 2013;9(4):409–414

54. Herndon CD, Ferrer FA, Freedman A, McKenna PH. Consensus on the prenatal management of antenatally detected urological abnormalities. *J Urol*. 2000;164 (3 Pt 2):1052–1056

55. Calaway AC, Whittam B, Szymanski KM, et al. Multicystic dysplastic kidney: is an initial voiding cystourethrogram necessary? *Can J Urol*. 2014;21(5):7510–7514

56. Timberlake MD, Herndon CDA. Mild to moderate postnatal hydronephrosis—grading systems and management. *Nat Rev Urol*. 2013;10(11):649–656

CHAPTER 11

Pediatric Urolithiasis

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Introduction

Incidence and Prevalence

Pediatric urolithiasis has become more common in the United States over the past several decades. There have been increasing numbers of emergency department visits, inpatient admissions, referrals, and outpatient surgeries. In the Rochester Epidemiology Project, Dwyer et al found an increasing incidence of urolithiasis, from 13 per 100,000 person-years between 1984 and 1990 to 36 per 100,000 person-years between 2003 and 2008 among children in Olmsted County, MN. The incidence increased by 4% per year during this 25-year period, with the greatest increase occurring in adolescents between 12 and 17 years of age. The etiologic origin for this increasing incidence is unknown. A variety of theories have been suggested, including the more commonplace detection of asymptomatic stones owing to the widespread use of imaging studies, changing referral patterns, the obesity epidemic, and climate change.

Genetic Factors

A variety of rare inborn errors of metabolism predispose the patient to urolithiasis, including cystinuria, Lesch-Nyhan syndrome, primary hyperoxaluria, and others. As the most common of these conditions,

cystinuria is estimated to account for 5% of children with urolithiasis. It is characterized by a defect in the proximal tubular reabsorption of filtered cystine, a homodimer of the amino acid cysteine. These conditions should be suspected in children with any of the following symptoms: early onset of urolithiasis before puberty, recurrent episodes of symptomatic stones, growth retardation, strong family history of urolithiasis and/or unexplained chronic kidney disease, and large burden of stones on imaging studies (multiple and bilateral stones, nephrocalcinosis). With the advent of modern sequencing technology, a growing number of polymorphisms are also being identified for more common causes of urolithiasis, such as idiopathic hypercalciuria.

Age, Sex, and Race

Older age is associated with a greater risk of urolithiasis, even in the pediatric population. By using a national database of inpatient admissions in 2003, Novak et al reported a higher prevalence of urolithiasis in adolescents than in younger children. The distribution of inpatient admission also varied according to patient sex, with a male predominance in the first decade after birth and female predominance in the second decade after birth. Overall, the prevalence of urolithiasis was higher in female children than in male children. There is also a racial variation in the risk of urolithiasis, with white children having the highest risk of urolithiasis, followed by Hispanic and African American children.

Obesity

While the association between obesity and urolithiasis is well established in adults, the evidence is sparse and conflicting in the pediatric population.

Geography and Climate

The temporal and geographic variation in the risk of urolithiasis has long been recognized in adults. An increased risk of urolithiasis is often identified during the warmer months and in geographic regions with hot, arid, and/or dry climates because of heat-induced sweating from a high ambient temperature. Whether this is a risk factor in the pediatric population requires further investigation. However, those in the pediatric population may be vulnerable because of their immature thermoregulatory systems and their dependence on caregivers.

Anatomic and Functional Abnormalities of the Urinary Tract

A neurogenic bladder from spinal cord or pelvic pathologic processes is associated with a risk of kidney and bladder stones from urinary stasis and recurrent urinary tract infections (UTIs). Continent lower urinary tract reconstruction (eg, bladder augmentation) with the incorporation of bowel into the urinary tract typically leads to bacteriuria and mucosuria, both of which predispose the patient to urolithiasis. Anatomic or functional abnormalities of the upper urinary tract are also thought to be associated with an increased risk of urolithiasis because of urinary stasis and recurrent UTIs. Common abnormalities of the upper and lower urinary tract associated with an increased risk of urolithiasis are provided in **Box 11-1**. These types of abnormalities are identified in up to 25% of children with urolithiasis.

Box 11-1. Common Medical and Surgical Conditions Associated With Urolithiasis

Acute tubular necrosis	Hyperthyroidism
Autosomal-dominant polycystic kidney disease	Ileostomy
Bariatric surgery	Immobilization
Chronic diarrheal states	Medullary sponge kidney
Chronic pancreatitis	Neurogenic bladder
Crohn disease	Primary hyperparathyroidism
Cystic fibrosis	Recurrent urinary tract infections
Diabetes mellitus type 2	Sarcoidosis
Disorders of bone demineralization (eg, rickets)	Seizure disorders
Distal renal tubular acidosis	Short bowel (gut) syndrome
Gout	Tumor lysis syndrome
Horseshoe kidney	Ulcerative colitis
	Ureteropelvic junction obstruction
	Ureterovesical junction obstruction

Pathophysiology

The pathophysiology of urolithiasis has been primarily investigated in adults. Although not completely understood, 4 mechanisms have been proposed: growth of calcium oxalate stones on exposed interstitial plaques of hydroxyapatite (known as *Randall plaque*), growth of stones on plugs in Bellini ducts, formation of cystine stones in dilated inner medullary collecting ducts, and crystallization of stones in free solution. All these mechanisms generally require a supersaturation of urinary solutes because of an increased renal secretion and/or a decreased urine volume, as well as a decreased concentration of inhibitors (eg, citrate) to promote the formation of stones. Growth on Randall plaques is likely the most important mechanism. As the most common group of stone formers, patients with idiopathic hypercalciuria primarily form calcium oxalate stones via this mechanism.

Diagnosis and Evaluation

The evaluation and diagnosis of children with suspected urolithiasis include a complete history, physical examination, and appropriate laboratory and imaging studies.

History

The clinical presentation of children with urolithiasis is variable, depending on their age and development. Pain is the most common symptom and is caused by ureteral obstruction and subsequent distention of the collecting system and/or renal capsule. While the classic symptoms of renal colic (ie, severe crampy flank pain radiating to the ipsilateral groin) are typically present in older adolescents, they are rarely present in younger children. Pain is often less severe and nonspecific or completely absent in the latter. Similar to younger children, the clinical presentation of those with developmental delay or other neurological diagnoses may be atypical and can even include increased seizure activity. Other possible symptoms include irritability, nausea, vomiting, poor oral intake, urinary frequency, urgency, dysuria, and gross hematuria. Lower urinary tract symptoms, such as frequency, urgency, and dysuria, suggest a concomitant UTI and/or obstruction

by the stone at the ureterovesical junction (UVJ). It is also important to elicit a history of fevers and document the temperature during the initial evaluation, as this finding can alter the acute management of symptomatic stones. A history of gross hematuria or recurrent UTIs can be the only indication that a further evaluation for urolithiasis should be performed. With the widespread use of imaging studies, the incidental finding of asymptomatic renal stones is becoming more common, as stated earlier.

The remaining history should be focused on the diet, past medical and surgical history, family history, and medications. A detailed dietary history includes the intake of sodium, calcium, oxalate-containing foods, and animal protein; fluid intake; over-the-counter supplements; and any specific diets. Certain diets are also associated with an increased risk of urolithiasis, such as the Atkins diet and the South Beach Diet for weight loss and the ketogenic diet for seizure disorders. Reviewing the past medical and surgical history, family history, and medications is important to identify any underlying causes and modifiable risk factors for urolithiasis. Common medical and surgical conditions, as well as medications associated with an increased risk of urolithiasis, are provided in **Boxes 11-1** and **11-2**, respectively. The anti-seizure medication most notable for stone formation is topiramate.

Box 11-2. Common Medications Associated With Urolithiasis

Crystallization of Drug	Metabolic Effect of Drug
Ephedrine	Acetazolamide
Indinavir	Allopurinol
Magnesium trisilicate antacids	Calcium
Triamterene	Corticosteroids
Trimethoprim-sulfamethoxazole	Furosemide
Zonisamide	Laxatives
	Topiramate
	Vitamin C
	Vitamin D

Physical Examination

A focused physical examination of children with suspected urolithiasis includes an assessment of vital signs, anthropometric measurements, general examination, and abdominal and/or flank and genital examination. A documented fever suggests a concomitant UTI and may alter the acute management of symptomatic stones. Tachycardia and hypertension can be present with pain, while tachycardia without or with hypotension suggests a compensated and decompensated shock, respectively. Hypertension and growth retardation may also indicate the presence of chronic kidney disease. A general examination is valuable in determining the severity of illness. In contrast to children with peritonitis, those with an acute symptomatic stone are typically writhing in pain and unable to find a comfortable position. Observing the patient's color, level of alertness, interaction with the parents and examiner, and quantity of tears with crying can also be used to assess the patient's mental status and level of hydration. The abdomen and flank are the most important component of the examination because of the wide differential diagnosis that accompanies symptoms of urolithiasis. The location and severity of tenderness vary on the basis of the size and location of stones, as well as the degree and acuity of ureteral obstruction. Tenderness from obstructing stones in the renal calyces and pelvis is often localized to the costovertebral angle, while that from obstructing distal ureteral stones is localized to the lower quadrants and the scrotum or the labia majora. A genital examination should be performed, since a variety of abdominal pathologic processes can manifest with referred scrotal pain and vice versa. Last, the extremities are examined for any bony abnormalities and edema.

Laboratory Studies

A dipstick analysis and microscopic urinalysis are performed in the initial evaluation of children with suspected urolithiasis. Red blood cells are typically present, although the absence of red blood cells does not preclude the presence of stones. Signs of UTI may also be present, including white blood cells and a high urinary pH level (due to urea-splitting bacteria). These findings are interpreted in the context of other signs and symptoms, such as a history of fevers and leukocytosis at a complete blood cell count. Urinary pH level is useful in

determining the composition of stones (eg, uric acid stones with a low urinary pH level, calcium phosphate stones with a high urinary pH level).

If a urinalysis result is suggestive of a UTI, a urine culture is performed. A UTI is among the differential diagnoses of flank and abdominal pain but can also be present concomitantly and alter the acute management of symptomatic stones. Of note, an obstructing ureteral stone associated with a febrile UTI is a worrisome situation that can lead to sepsis and shock if not promptly addressed.

Additional serum studies are selectively performed, depending on the clinical circumstances. A complete blood cell count may be helpful to assess the patient for leukocytosis if there is clinical suspicion of a UTI. However, an increased white blood cell count is not always indicative of UTI and can be present with pain, stress, and inflammation. A renal panel may also be used to evaluate the patient for acute kidney injury in the setting of dehydration, bilateral obstructing stones, and an obstructing stone in a solitary kidney.

The composition of any passed or removed stone should be analyzed on at least one occasion, with repeat analysis considered for children with recurrent urolithiasis that is refractory to dietary and/or pharmacological therapies. Knowledge of stone composition is important in adapting the treatment regimen.

At the authors' institution, all children undergo a urinary and serum metabolic evaluation, since up to 70% of children with urolithiasis have a metabolic abnormality. This evaluation is performed after patients have recovered from an acute symptomatic stone and have returned to their normal state of health. It consists of a renal panel, serum uric acid level, serum parathyroid hormone level (if there is an increased serum calcium level), and one or two 24-hour urine collections, which should be obtained with the patient on a random diet and analyzed at a minimum for total volume, pH level, and calcium, oxalate, uric acid, citrate, sodium, potassium, and creatinine levels. A random (spot) urinary calcium-to-creatinine ratio is also a simple screening test for hypercalciuria. A ratio higher than 0.2 mg/kg is considered abnormal for children older than 1 year and should prompt a 24-hour urine collection. However, a value within reference range does not necessarily rule out hypercalciuria, since the urine calcium level may vary during the day.

Imaging Studies

The choice of imaging studies in children with suspected urolithiasis is centered on minimizing their exposure to ionizing radiation and cumulative risk of secondary cancers. While nonenhanced computed tomography (CT) of the abdomen and pelvis is the standard of reference for identification of kidney stones in adults, it is used selectively in children. Ultrasonography (US) is the imaging study of choice in the pediatric population (**Figure 11-1**).

The benefits of US include its accessibility, cost, and lack of ionizing radiation. US is particularly useful in determining the presence of ureteral obstruction with hydronephrosis and/or lack of a ureteral jet. However, it is operator dependent and less accurate in determining the burden of stones. US tends to allow overestimation of the size of stones and can cause smaller stones to be missed. It is particularly helpful in showing obstruction (hydronephrosis), which is an important factor to consider when making a decision on the disposition of a patient during an acute stone episode. It is important to remember that the absence of hydronephrosis does not preclude obstruction. Also, US is poor at visualizing the ureter, so obstructing ureteral stones may be missed. Abdominal radiography is an additional option but is limited in the identification of radiolucent stones (eg, uric acid stones) and smaller stones that are obscured by overlying structures and bowel gas. US has a sensitivity of 76% and a specificity of 100% when compared to CT, but the decreased sensitivity of US rarely leads to a change in management. CT can still be indicated in certain circumstances, particularly when the findings at US and/or abdominal radiography are equivocal and may change the management or when a more detailed understanding of the anatomy is needed for surgical planning.

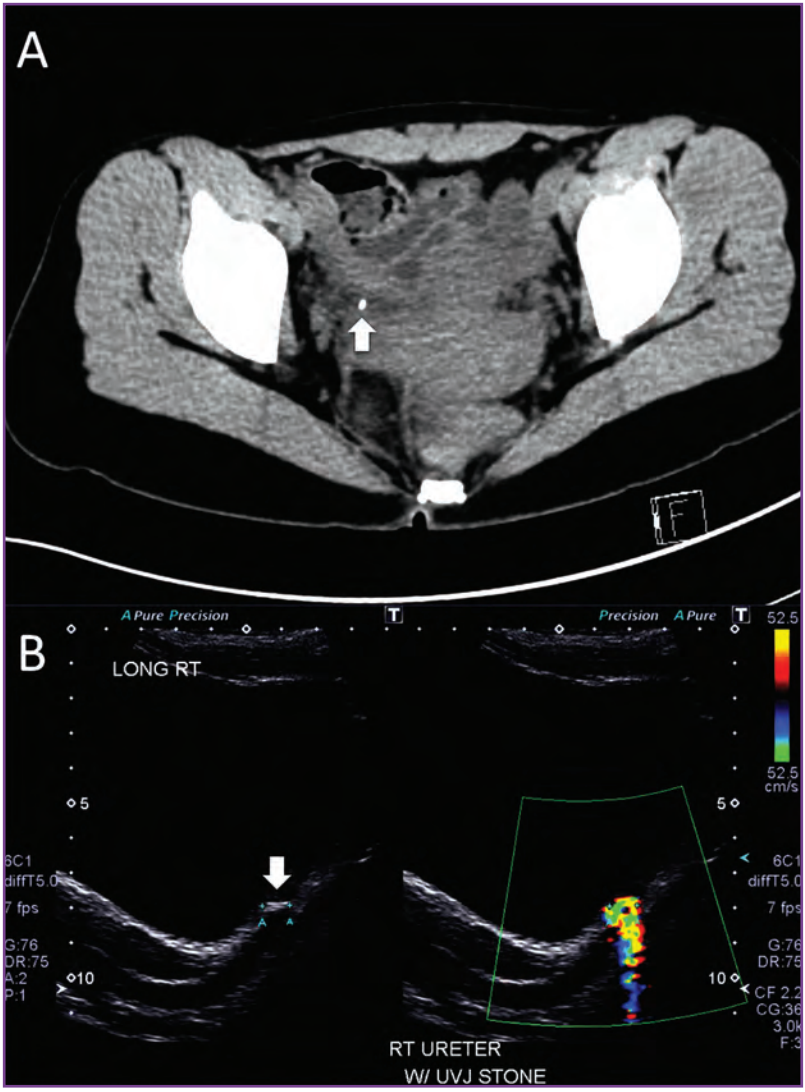

Figure 11-1. Computed tomography (CT) and ultrasonography (US) in a 16-year-old female patient with right renal colic. **A,** Nonenhanced axial CT of the abdomen and pelvis was initially performed at a local hospital and demonstrated a 5-mm stone in the right distal ureter (arrow) with mild right hydroureteronephrosis. **B,** Doppler renal and bladder US was performed for worsening symptoms about 1 week later and demonstrated the stone at the right ureterovesical junction (arrow), with twinkle artifact on Doppler images and slightly increased right hydroureteronephrosis. The patient ultimately underwent right ureteroscopy with laser lithotripsy and stone basket extraction because of a failure of medical expulsive therapy.

Treatment Options and Outcomes

The initial goal in the acute management of symptomatic stones is a safe, timely, and cost-effective treatment plan. The long-term goal is the identification of underlying causes and modifiable risk factors to decrease the risk of recurrence and adverse sequelae, such as chronic renal insufficiency. An underlying cause or modifiable risk factor is more commonly identified in the pediatric population than in the adult population.

Acute Management

The acute management of symptomatic stones depends on the severity of symptoms, as well as the presence of ureteral obstruction and UTI. A trial of spontaneous passage with hydration and analgesic therapy is indicated for prepubertal children with ureteral stones up to 4 mm and postpubertal adolescents with ureteral stones up to 6 mm, although spontaneous passage is possible with ureteral stones up to 10 mm. Pain is best controlled with a combination of narcotic medications and nonsteroidal anti-inflammatory drugs (NSAIDs). Narcotic medications may be omitted in young children, while NSAIDs are avoided in the setting of chronic kidney disease and/or acute kidney injury. NSAIDs should also be used with caution in the child who is vomiting and/or dehydrated. Medical expulsive therapy (MET) with α-adrenergic antagonists (eg, tamsulosin, doxazosin) or calcium channel blockers (eg, nifedipine) has been increasingly used to facilitate the spontaneous passage of ureteral stones, as well. These medications relax the smooth muscle within the ureter, leading to an inhibition of ureteral spasm and contraction. A meta-analysis demonstrated that MET with α-adrenergic antagonists (tamsulosin 0.4 mg or doxazosin 0.03 mg/kg/d) significantly increased the odds of spontaneous passage for stones with a mean size of 3 to 8 mm (odds ratio, 2.21; 95% confidence interval, 1.84–8.95). Most children tolerated α-adrenergic antagonists, with fewer than 1% discontinuing use because of adverse effects. Mild adverse effects occurred in up to 4% of children, including somnolence, dizziness, headache, nausea, and vomiting. The role of MET is much better defined for distal than middle or proximal ureteral stones but may still be considered for these stones, given the limited adverse effects in the pediatric population. Families should be informed that the use of α-adrenergic

antagonists to facilitate the spontaneous passage of ureteral stones is an "off-label" indication.

A trial of spontaneous passage can typically be managed in the outpatient setting, as long as the child is hydrated and able to take oral analgesics. Close follow-up is warranted to ensure a successful passage of stones over several weeks. A trial of spontaneous passage should not exceed 6 weeks to avoid irreversible kidney injury. Instructions are provided to strain all urine output to document the spontaneous passage of stones and obtain a specimen for analysis. Imaging studies may be repeated prior to any surgical intervention if the symptoms have changed, suggesting a change in the position or spontaneous passage of stones that can influence the choice of surgical options or need for surgery. Indications for inpatient admission include dehydration, poorly controlled pain, impaired renal function, and evidence of UTI.

The likelihood of spontaneous passage correlates with the size and location of stones, with larger and more proximal stones being less likely to pass spontaneously. Although the natural history of urolithiasis is not as clearly defined in the pediatric population, most ureteral stones smaller than 5 mm will pass spontaneously.

Surgical Intervention

Given the relatively high rate of spontaneous passage, as well as the cost and potential complications of surgery, a period of observation is generally recommended prior to any surgical intervention for uncomplicated stones up to 10 mm in diameter. Indications for surgery are provided in **Box 11-3**.

Box 11-3. Indications for Surgery

Intractable nausea and/or vomiting
Poorly controlled pain
Acute kidney injury
Obstruction in the setting of urinary tract infection
Bilateral obstructing stones or obstructing stone in a solitary kidney
Failed trial of spontaneous passage with or without medical expulsive therapy
Stones >10 mm in diameter

As previously mentioned, ureteral obstruction in the setting of UTI can become a surgical emergency because of the potential for sepsis. Urgent decompression may be achieved with the placement of a retrograde ureteral stent by a urologist via cystoscopy or a percutaneous nephrostomy tube, depending on the hemodynamic stability, size, and location of stones and the availability of an interventional radiology service comfortable with the procedure in children.

For children in whom a trial of spontaneous passage is chosen with or without MET, the maximum duration of observation is not clearly defined but should not exceed 6 weeks, on the basis of experimental data on the development of irreversible kidney injury from ureteral obstruction. A shorter duration can also be offered by using a shared decision-making approach. For children with asymptomatic renal stones, a period of active surveillance is an option but requires regular follow-up with serial imaging studies to monitor the patient for an increase in the size and/or number of stones, as well as the development of silent ureteral obstruction. If an observational approach is selected, it is helpful to counsel families that kidney stones are unpredictable and that renal colic can sometimes occur at inconvenient times and settings.

As previously mentioned, a ureteral stent can be placed in the acute setting to relieve the obstruction. Surgery for definitive treatment of stones can be subsequently performed, unless the stones are readily accessible in the initial setting. A ureteral stent typically improves the symptoms of renal colic but may be poorly tolerated because of urinary frequency, urgency, dysuria, a sensation of incomplete emptying, and stent-related bladder discomfort. These symptoms can be minimized with anticholinergic medications (eg, oxybutynin) and/or α-adrenergic antagonists (eg, tamsulosin, doxazosin).

Surgical options for the definitive treatment of stones include extracorporeal shock wave lithotripsy, ureteroscopy, or percutaneous nephrolithotomy. Additional information on these surgical options is summarized in **Table 11-1**.

These surgical options have largely replaced the open removal of stones. A minimally invasive approach with laparoscopy or robotic assistance may be indicated in certain circumstances, particularly in the setting of a concomitant stone and anatomic abnormality (eg, ureteropelvic junction obstruction, UVJ obstruction, ectopic ureter) necessitating a surgical repair. Otherwise, clinicians should not routinely perform

Table 11-1. Surgical Options for Urolithiasis

Surgery	General Description	Indications	Stone-Free Rates	Limitations	Complications
Extracorporeal shock wave lithotripsy	Noninvasive procedure for fragmentation of stones with high-energy shock waves	All ureteral and renal stones; there is a need for a ureteral stent or nephrostomy tube in stone burden >20 mm.	Ureteral stones <10 mm: 87% Ureteral stones >10 mm: 73% Renal stones <20 mm: 80%–85% Renal stones >20 mm: 73%–83%	Access to lithotripter, higher rate of repeat treatment	Bleeding, Steinstrasse (collection of fragments causing ureteral obstruction), UTI
Ureteroscopy	Endoscopic procedure with retrograde insertion of ureteroscope into the bladder and up the ureter and into the kidney for fragmentation and/or extraction of stones	Ureteral stones, renal stones <20 mm	Ureteral stones <10 mm: 95% Ureteral stones >10 mm: 78% Renal stones <20 mm: 85%	Greater technical expertise, difficulty in accessing small-caliber ureter, pre- and postoperative stent placement	Bleeding, ureteral perforation and/or avulsion, ureteral obstruction, UTI, ureteral stricture, inability to remove all stone burden

Continued

Table 11-1 (*continued*)

Surgery	General Description	Indications	Stone-Free Rates	Limitations	Complications
Percutaneous nephrolithotomy	Procedure with percutaneous access to the kidney and anterograde insertion of a renoscope for fragmentation and/or extraction of stones	Renal stones >20 mm	Renal stones >20 mm: 90%	More invasive, higher rate of complications, inpatient admission	Bleeding, renal perforation, ureteral obstruction, UTI, colonic injury, pneumothorax, hydrothorax

Abbreviation: UTI, urinary tract infection.

open, laparoscopic, or robotic surgery for upper tract urinary stones in children. The choice of surgical options depends on several factors, including body habitus, size and location of stones, composition of stones, anatomy of the collecting system, concomitant anatomic and functional abnormalities, proximity of surrounding structures, surgeon preference, and availability of equipment. Extracorporeal shock wave lithotripsy and ureteroscopy are generally indicated for smaller renal and ureteral stones, while percutaneous nephrolithotomy is indicated for larger (>2 cm) or branched renal stones. Dense renal stones (eg, calcium oxalate monohydrate or cysteine) may also benefit from a percutaneous renal procedure. A ureteral stent is often placed after ureteroscopy to allow for clearance of residual fragments and prevent obstruction from edema. It is typically removed within 1 week of surgery by gently pulling on an attached string that is externalized through the urethra. If the string is removed from the stent at the time of surgery, it becomes necessary to perform cystoscopy under anesthesia for stent removal.

Prevention

Prevention is the most effective treatment of children with urolithiasis, given the high incidence of underlying causes and modifiable risk factors. Children with a medical or surgical condition associated with an increased risk of urolithiasis should be appropriately treated (see **Box 11-1**). In children who are taking a medication associated with an increased risk of urolithiasis, the prescribing physician should also discuss its discontinuation and initiation of an alternative medication, if feasible (see **Box 11-2**).

General dietary recommendations are provided to all children with a history of urolithiasis. A minimum fluid intake of 1.5 to 2.0 L/m^2/d is recommended to decrease the supersaturation of urinary solutes. The fluid intake should be adjusted to maintain a 24-hour urine volume of 750 mL in infants, 1,000 mL in children younger than 5 years, 1,500 mL in children between 5 and 10 years of age, and 2,000 mL in children older than 10 years. Sugar-sweetened beverages should be avoided because of their association with an increased risk of urolithiasis, particularly phosphoric acid–based sodas. Lemonade is widely recommended for patients with kidney stones because it contains citrate, a known calcium stone inhibitor.

Children are also instructed to follow the recommended dietary allowance of calcium for their age. A dietary restriction of calcium, although counterintuitive, should be avoided, because it leads to an increased intestinal absorption of oxalate and increases the risk of calcium oxalate stones. Children are instructed to avoid a high intake of sodium and nondairy animal protein, as well. A high intake of sodium leads to hypercalciuria because of the decreased reabsorption of calcium in the proximal tubule, while a high intake of nondairy animal protein leads to hypercalciuria and hypocitraturia because of a high acid load. However, a dietary restriction of nondairy animal protein below the recommended dietary allowance should also be avoided because of its potentially deleterious effects on growth and development. Patients with a history of calcium oxalate stones should moderate intake of oxalate-rich foods such as nuts, chocolate, and dark leafy greens. Finally, an increased intake of fruit and vegetables is recommended. Both are excellent sources of potassium and citrate, which are stone inhibitors.

Pharmacological therapy is considered for children who are unresponsive to dietary modifications and those who have a high risk of recurrence (eg, inborn errors of metabolism) and adverse sequelae (eg, solitary kidney). This is often managed by a pediatric nephrologist. The primary medications include thiazide diuretics (eg, hydrochlorothiazide, chlorthalidone) and potassium citrate, both of which are well tolerated, with minimal adverse effects in children. Thiazide diuretics are indicated in children with recurrent calcium stones and hypercalciuria. They increase the reabsorption of calcium in the distal tubule, leading to a decreased excretion of calcium. Conversely, potassium citrate is indicated in children with recurrent calcium stones and hypocitraturia. It is also indicated in children with uric acid and cystine stones, since urinary alkalinization inhibits the formation of these stones. Both medications can be considered in children with recurrent calcium stones but absent or appropriately addressed metabolic abnormalities, as well. Other indications for pharmacological therapy include the use of allopurinol in children with recurrent calcium oxalate stones and hyperuricosuria or recurrent uric acid stones that are refractory to urinary alkalinization, as well as the use of cystine-binding thiol medications (eg, α-mercaptopropionylglycine) in children with cystinuria who are unresponsive to dietary modifications and urinary alkalinization.

Appropriate serum studies and a single 24-hour urine collection are repeated within 6 months of dietary and/or pharmacological therapies to assess the adherence of families and guide any further adjustments. Children who are taking a thiazide diuretic are specifically monitored for hypokalemia and are often required to take a potassium supplement, while those taking potassium citrate are monitored for hyperkalemia and excessive urinary alkalinization, the latter of which may increase the risk of calcium phosphate stones. After the initial follow-up, a single 24-hour urine collection and an appropriate imaging study are repeated on at least an annual basis, depending on the frequency of recurrent episodes.

When to Refer

- All children with urolithiasis should be referred to a pediatric urologist and possibly a pediatric nephrologist, to determine whether surgical intervention may be required.
- Referral should occur soon after the initial diagnosis is established in children with an acutely symptomatic or incidentally detected kidney stone.
- Children with a history of urolithiasis should be referred, to decrease the risk of recurrence and adverse sequelae in the future.
- If available, pediatric urolithiasis is ideally managed in a multidisciplinary stone center with urologists, nephrologists, registered dietitians, geneticists, and nursing coordinators. An improved outcome for children with urolithiasis will hopefully be achieved with a comprehensive and coordinated approach to care.

Clinical Pearls

- While the classic symptoms of renal colic are typically present in older adolescents, they may not be present in younger children.
- It is important to elicit a history of fevers and identify signs of a UTI during the initial evaluation, since these findings can alter the acute management of symptomatic stones.
- US is the initial imaging study of choice in children with suspected urolithiasis. Nonenhanced CT of the abdomen and pelvis is reserved for certain circumstances in which the US findings are equivocal and may change the management.

- An outpatient trial of spontaneous passage with hydration, analgesic therapy, and MET is indicated for children with uncomplicated ureteral stones of an appropriate size to pass.
- A period of observation is generally recommended prior to any surgical intervention. Indications for surgery include intractable nausea and/or vomiting, poorly controlled pain, acute kidney injury, ureteral obstruction in the setting of UTI, bilateral obstructing stones or obstructing stone in a solitary kidney, and failed trial of spontaneous passage. Non-obstructing stones larger than 1 cm typically require surgical intervention, given the low likelihood of passage and risk of complications if left untreated.
- Given the high incidence of underlying causes and modifiable risk factors, children should undergo a metabolic evaluation to decrease the risk of recurrence and adverse sequelae.

Resources for Parents

- U.S. Department of Health and Human Services, National Institute of Diabetes and Digestive and Kidney Diseases. Kidney stones in children. https://www.niddk.nih.gov/health-information/urologic-diseases/kidney-stones/children. Accessed October 17, 2018
- Smith J, Stapleton FB. Patient education: kidney stones in children (Beyond the Basics). UpToDate Web site. https://www.uptodate.com/contents/kidney-stones-in-children-beyond-the-basics. Reviewed September 2018. Accessed October 17, 2018

Suggested Readings

Pearle MS, Goldfarb DS, Assimos DG, et al; American Urological Association. Medical management of kidney stones: AUA guideline. *J Urol*. 2014;192(2):316–324

Tasian GE, Copelovitch L. Evaluation and medical management of kidney stones in children. *J Urol*. 2014;192(5):1329–1336

Hernandez JD, Ellison JS, Lendvay TS. Current trends, evaluation, and management of pediatric nephrolithiasis. *JAMA Pediatr*. 2015;169(10):964–970

Assimos D, Krambeck A, Miller NL, et al. Surgical management of stones: American Urological Association/Endourological Society guideline, part I. *J Urol*. 2016;196(4):1153–1160

References

1. Dwyer ME, Krambeck AE, Bergstralh EJ, Milliner DS, Lieske JC, Rule AD. Temporal trends in incidence of kidney stones among children: a 25-year population based study. *J Urol*. 2012;188(1):247–252
2. Pearle MS, Antonelli JA, Lotan Y. Urinarly lithiasis: etiology, epidemiology, and pathogenesis. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 11th ed. Philadelphia, PA: Elsevier; 2016:1170–1199
3. Novak TE, Lakshmanan Y, Trock BJ, Gearhart JP, Matlaga BR. Sex prevalence of pediatric kidney stone disease in the United States: an epidemiologic investigation. *Urology*. 2009;74(1):104–107
4. Evan AP, Worcester EM, Coe FL, Williams J Jr, Lingeman JE. Mechanisms of human kidney stone formation. *Urolithiasis*. 2015;43(Suppl 1):19–32
5. Kovacevic L, Wolfe-Christensen C, Edwards L, Sadaps M, Lakshmanan Y. From hypercalciuria to hypocitraturia—a shifting trend in pediatric urolithiasis? *J Urol*. 2012;188(4 Suppl):1623–1627
6. Pearle MS, Goldfarb DS, Assimos DG, et al; American Urological Assocation. Medical management of kidney stones: AUA guideline. *J Urol*. 2014;192(2):316–324
7. Tasian GE, Copelovitch L. Evaluation and medical management of kidney stones in children. *J Urol*. 2014;192(5):1329–1336
8. Fulgham PF, Assimos DG, Pearle MS, Preminger GM. Clinical effectiveness protocols for imaging in the management of ureteral calculous disease: AUA technology assessment. *J Urol*. 2013;189(4):1203–1213
9. Passerotti C, Chow JS, Silva A, et al. Ultrasound versus computerized tomography for evaluating urolithiasis. *J Urol*. 2009;182(4 Suppl):1829–1834
10. Assimos D, Krambeck A, Miller NL, et al. Surgical management of stones: American Urological Association/Endourological Society guideline, part I. *J Urol*. 2016;196(4):1153–1160
11. Velázquez N, Zapata D, Wang HH, Wiener JS, Lipkin ME, Routh JC. Medical expulsive therapy for pediatric urolithiasis: systematic review and meta-analysis. *J Pediatr Urol*. 2015;11(6):321–327
12. Schneck FX, Ost MC. Surgical management of pediatric stone disease. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 11th ed. Philadelphia, PA: Elsevier; 2016:3102–3120

CHAPTER 12

Urological Oncology in Pediatrics

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Kidney

Wilms Tumor

Introduction

Wilms tumor (WT) is the most common renal tumor in children, and it is the second most common abdominal tumor in children. The Children's Oncology Group (COG) provides treatment guidelines, tumor registries, and clinical trials for WT in North America. This group advocates for early removal of the primary tumor to examine the histologic findings, followed by adjuvant therapy when necessary. In the United States, children and adolescents are treated per the COG guidelines, and it is important to have early involvement of a pediatric oncologist who is familiar with COG guidelines, protocols, and studies when caring for children with WT.

WT accounts for 85% of all pediatric renal tumors (**Table 12-1**), with approximately 500 new cases of WT diagnosed annually in the United States. The typical age at diagnosis is 3 to 5 years, with 95% of WT cases diagnosed before 10 years of age. Patients with syndromes that

Table 12-1. Incidence Rates of Pediatric Renal Tumors

Tumor Type	Frequency
Wilms tumor	85%
Congenital mesoblastic nephroma	5%
Clear cell sarcoma	4%
Rhabdoid tumor	2%
Miscellaneous	4%

predispose them to developing WT and bilateral disease tend to present at a younger age. African American patients are at higher risk for developing WT than white patients, and the Asian population appears to have the lowest risk.

Multiple genes have been implicated in the development of WT. The *WT1* gene that encodes the WT protein is a tumor suppressor gene located on the short arm of chromosome 11. This gene encodes a transcription factor involved with normal development of the urogenital system. When both copies of *WT1* are mutated, WT can develop. Mutations in *WT1* and regions close to it can lead to WT predisposition syndromes (summarized in **Table 12-2**), along with unique physical findings. For example, *PAX6* is a gene located near the *WT1* gene and, when mutated, this can result in aniridia.

Evidence for screening patients at high risk for the development of WT, such as those with Beckwith-Wiedemann syndrome, is mixed—some studies demonstrate an improvement with screening detection of WT because of lower tumor stage at diagnosis, while others show no difference. A screening protocol of abdominal ultrasonography (US) performed every 3 to 4 months for the first 7 years after birth has generally been adopted. Patients who develop a unilateral renal mass and have syndromes that predispose them to developing WT are treated with slightly different preoperative chemotherapy regimens, and early involvement of a pediatric oncologist to help with nuanced treatment regimens is recommended.

Table 12-2. Syndromes That Predispose Patients to Developing Wilms Tumor

Syndrome	Genetics	Associated Features	Risk of Wilms Tumor
WAGR	11p13 *WT1*, *PAX6*	Wilms tumor Aniridia Genital abnormalities (DSD) Intellectual disability	50%
Denys-Drash	*WT1*	Wilms tumor Genital abnormalities (DSD) Renal failure/nephropathy (mesangial sclerosis)	90%
Beckwith-Wiedemann	11p15.5	Prenatal and postnatal overgrowth Hemihypertrophy (growth asymmetry) Macroglossia Anterior abdominal wall defects Ear creases, pits	7%
Frasier	*WT1*	Nephropathy (FSGS) DSD Gonadoblastoma Wilms tumor	6%

Abbreviations: DSD, disorder of sex development; FSGS, focal segmental glomerulonephritis; WAGR, Wilms tumor, aniridia, genitourinary malformations, and intellectual disability.

Evaluation

Patients classically present with a palpable mass or gross hematuria, but abdominal pain and hypertension have been reported, as well. Rarely, children with WT receive diagnoses incidentally at imaging, performed for another reason.

Imaging should begin with renal US. This will confirm a solid renal mass and can also be used for preliminary evaluation of the contralateral kidney. Subsequent imaging consists of computed tomography (CT) of the chest, abdomen, and pelvis with intravenous (IV) contrast material administered in a single setting (**Figure 12-1**).

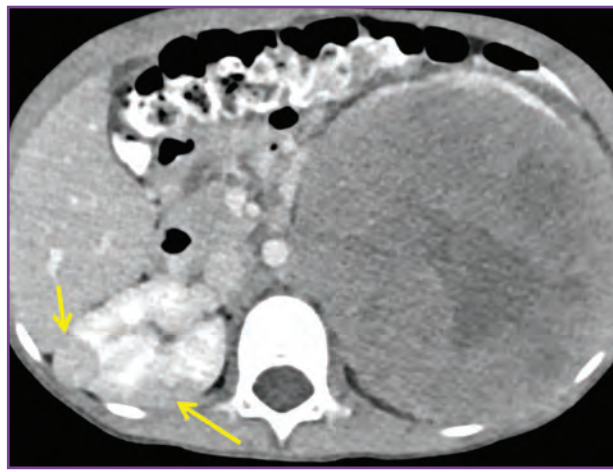

Figure 12-1. Axial computed tomography of the abdomen and pelvis performed with intravenous contrast material shows a large left renal mass and small right renal masses (arrows).

This minimizes the radiation a child receives, while allowing complete preoperative staging. Laboratory workup should include a complete blood cell count, liver function panel, basic metabolic panel, urinalysis, and coagulation panel. This strategy is used to investigate the presence of anemia and increased liver enzyme levels and allows the potential detection of acquired von Willebrand disease, which is reported to occur in up to 2% of patients with WT.

Diagnosis and Treatment

Up-front radical nephrectomy with lymph node (LN) sampling is the mainstay of initial treatment of unilateral, nonsyndromic tumors, even in patients with metastatic disease. There are, however, cases when early surgery is not possible, such as when the disease is deemed unresectable

(invasion of the surrounding organs, tumor thrombus in the inferior vena cava extending above the hepatic veins, or overwhelming pulmonary or hepatic metastatic involvement making surgery unsafe). Open resection is the mainstay of surgical intervention, since there is concern for tumor rupture, adequate staging, and port-site tumor seeding in the less controlled setting of minimally invasive laparoscopic surgery. Preoperative tumor biopsy is rarely indicated per COG protocols and has serious treatment implications, since performing biopsy up front or starting chemotherapy prior to nephrectomy generally results in automatic local stage III designation. This stage mandates the addition of doxorubicin to the chemotherapy regimen and postoperative radiation therapy to the renal fossa, both of which are associated with clinically significant morbidity.

Nephron-sparing surgery (NSS; partial nephrectomy) is indicated only in the setting of bilateral tumors, a tumor in a solitary kidney, predisposition syndromes, and clinical trials. Typically, patients with such tumors will undergo preoperative chemotherapy, followed by attempted NSS to allow tumor shrinkage and preservation of as much normal renal tissue as possible. When a tumor is deemed unresectable, biopsy is performed, followed by presurgical chemotherapy, to allow shrinkage of the tumor to permit surgical resection. With the advances of cross-sectional imaging, the contralateral kidney can be well examined preoperatively by using CT. See **Table 12-3** for surgical management options.

In the early 20th century, survival for WT was dismal. With improvements in anesthesia and surgical techniques, survival increased to about 30% by the 1930s. With the advent of radiation therapy, followed by the addition of chemotherapy, the survival of these patients currently exceeds 90%. Even with relapse, salvage rates are high. Multiple genetic biomarkers have been identified for WT that can help further risk-stratify patients for closer monitoring or more intensive therapies. For example, patients with loss of heterozygosity at chromosomes 1p and 16q have an increased risk of relapse and death from WT.

Intensive follow-up with pediatric oncology is needed for these patients, both for disease monitoring and surveillance and for the development of long-term effects from therapy (eg, secondary malignancies and heart disease).

Table 12-3. Management Strategies for Favorable Histologic Wilms Tumor Findings on the Basis of Children's Oncology Group Protocols

Stage	Percentage of Tumors	Criteria	Therapy (Favorable Histologic Findings)[a]	Percentage of 4-y Survival
I	40%–45%	Confined to the kidney Negative margin No nodal involvement	Nephrectomy with LN sampling,[b] followed by vincristine and actinomycin	83%–99%
II	20%	Spread beyond the kidney Negative margins No nodal involvement	Nephrectomy with LN sampling,[b] followed by vincristine and actinomycin	81%–98%
III	20%–25%	Peritoneal tumor implants Positive margin Preoperative biopsy Preoperative chemotherapy Preoperative or intraoperative tumor rupture Piecemeal removal Nodal involvement	Nephrectomy with LN sampling,[b] followed by vincristine, actinomycin, and doxorubicin with abdominal external-beam radiation	72%–94%

Table 12-3 (*continued*)				
Stage	**Percentage of Tumors**	**Criteria**	**Therapy (Favorable Histologic Findings)[a]**	**Percentage of 4-y Survival**
IV	10%	Distant metastatic disease	Nephrectomy with LN sampling,[b] followed by vincristine, actinomycin, and doxorubicin with abdominal and lung external-beam radiation	38%–86%
V	5%	Bilateral tumors	Vincristine and actinomycin, followed by NSS/LN sampling	55%–87%

Abbreviations: LN, lymph node; NSS, nephron-sparing surgery.

[a] With unfavorable histologic findings, administer doxorubicin and external-beam radiation earlier (ie, with lower stages) and 5-drug chemotherapy if there are diffuse, unfavorable histologic findings.

[b] Preoperative chemotherapy is only indicated with unresectable primary tumor and/or abdominal disease.

Other Renal Tumors

Congenital Mesoblastic Nephroma

Congenital mesoblastic nephroma (CMN) is the most common renal tumor in infants younger than 6 months. It was originally described as a benign tumor, but recurrent and/or metastatic cases have been rarely reported. This is the most common tumor of newborns, with most cases diagnosed in the first 6 months after birth. CMN is slightly more common in male patients than female patients (ratio of 1.5:1). This tumor is proposed to be an abnormal proliferation of the nephrogenic mesenchyme during the fetal and/or neonatal period. Classically, CMN appears with a palpable mass at presentation in the newborn period. In some cases, it may be detected prenatally and may be associated with polyhydramnios and preterm birth (**Figure 12-2**).

Imaging studies (typically US) show this tumor to be confined to the kidney. It is usually large, with cystic, necrotic, and hemorrhagic areas. As with any renal mass that is concerning for malignancy, a full staging workup with CT of the chest, abdomen, and pelvis is indicated. A complete blood cell count and comprehensive metabolic panel are used for laboratory workup. Metastases are rare but have been reported to occur in the lung, brain, liver, heart, and bone.

Any patient younger than 6 months with a solid renal mass is assumed to have CMN (WT is much less likely in this age group), and radical nephrectomy is performed. LN sampling is advocated to obtain accurate

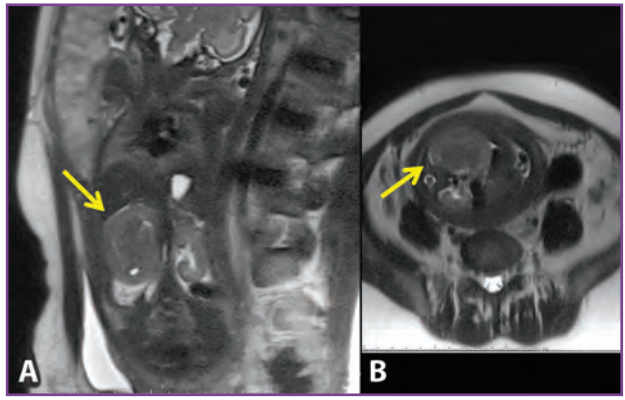

Figure 12-2. Sagittal (**A**) and axial (**B**) prenatal T2-weighted magnetic resonance images show a right renal mass (arrows).

staging information in the event that this is a WT. The rarity of the tumor and even more rare cases of recurrence make it difficult to identify risk factors for recurrence, but a positive surgical margin and the cellular subtype have been suggested. Overall prognosis is good, especially if treated in the first 6 months after birth. Recurrence and metastasis have been reported in small series but are truly unknown because of the rarity of this tumor. There is no established follow-up for CMN, but serial abdominal US for the first 2 years is advised.

Renal Cell Carcinoma

Renal cell carcinoma (RCC) is the second most common renal tumor in children and is the most likely diagnosis after 12 years of age. Median age at presentation is 12.9 years (range, 1.9–22.1 years). Because of the rarity of this tumor, there have been a few reports of an African American racial predominance and a predominance in female patients, with male patients presenting with more advanced disease and having worse outcomes—but this has not been completely elucidated. Staging is based on the TNM staging system as adults. The most common histologic subtype of RCC in children is translocation RCC, which accounts for 46.7% of pediatric cases. This type of tumor is associated with increased activity of the transcription factor TFE3 on Xp11.2. Additionally, multiple gene mutations have been associated with predisposing syndromes for other subtypes of RCC (**Table 12-4**).

Pediatric RCC tends to appear with hematuria, large masses, and advanced disease at presentation (56.4% of cases have nodal involvement or distant metastases). Metastatic sites include the lungs, liver, and bone.

Laboratory evaluation includes complete blood cell count, comprehensive metabolic panel, and urinalysis. CT of the chest, abdomen, and pelvis with IV contrast material administered in a single setting minimizes radiation exposure. Abdominal imaging is usually performed with CT, but magnetic resonance imaging can also be used.

Open radical nephrectomy is the preferred management for pediatric RCC. Laparoscopy and NSS have been described in adults and are likely to be adequate in the pediatric RCC population, but their application is limited, as children are treated under the assumption of having a renal mass due to WT. Up to 50% of children with RCC and tumor smaller than 4 cm have LN involvement. Therefore, a thorough retroperitoneal

Table 12-4. Syndromes That Predispose the Patient to Development of Renal Cell Carcinoma

Disease	Gene	Presentation
von Hippel-Lindau disease	3p; *VHL* tumor suppressor	Clear cell RCC Retinal and CNS hemangioblastomas Pheochromocytomas Pancreatic cysts, tumors Epididymal cystadenomas
Tuberous sclerosis	*TSC1* or *TSC2*	Angiomyolipoma Clear cell RCC Seizures Intellectual disability Facial angiofibromas Hamartomas
Hereditary papillary RCC	*MET* proto-oncogene	Low grade type 1 papillary RCC
Birt-Hogg-Dube syndrome	*FLCN* tumor suppressor	Chromophobe RCC Fibrofolliculomas Lung cysts and blebs
Hereditary leiomyomatosis and RCC	*FH* tumor suppressor	High-grade type 2 papillary RCC Uterine fibroids at young age
Succinate dehydrogenase RCC	*SDH*	Different RCCs Paragangliomas pheochromocytomas
Sickle cell disease and/or trait	*HbS*	Renal medullary carcinoma

Abbreviations: CNS, central nervous system; RCC, renal cell carcinoma.

LN dissection is recommended in children with RCC, even with small masses amenable to NSS. Additionally, if the tumor is WT and not RCC, this allows for adequate staging and subsequent management. There are limited data on adjuvant therapies for RCC. A recent study of the National Cancer Database indicates a 5-year overall survival (OS) rate

of 70% for all pediatric patients with RCCs. Patients without nodal involvement have an OS rate between 91% and 100%, patients with LN involvement have an OS rate of 71%, and patients with metastases have an OS rate of 8%. Tumor size, LN involvement, and lack of surgical resection are factors predictive of worse OS, emphasizing the important role surgical resection plays in the management of these patients. The patients undergo routine follow-up with cross-sectional imaging and laboratory studies similar to those for WT.

Rhabdoid Tumor

Rhabdoid tumor of the kidney is a rare, aggressive pediatric renal tumor. The exact cell type of derivation is unknown, and there are occasional occurrences of separate central nervous system primary tumors. Eighty percent of these tumors occur in children younger than 2 years, with a male predominance (ratio of 1.5:1 for male to female patients). Median age at diagnosis is 10.6 months. A large proportion of patients with rhabdoid tumor of the kidney have a germline mutation that predisposes them to this tumor. This mutation has incomplete penetrance, and family members may have gonadal mosaicism. This must be considered when counseling these patients and families. Hematuria is the typical symptom at presentation, but symptoms associated with metastatic disease (to the brain, lung, and liver) are present in up to 80% of cases. CT of the chest, abdomen, and pelvis is needed just like in other renal tumors. For rhabdoid tumor of the kidney, imaging of the central nervous system is performed at the time of diagnosis, given the high risk of metastatic disease to the brain. The development of central nervous system lesions is more common in patients younger than 1 year at diagnosis.

Early radical nephrectomy with LN dissection is the mainstay of treatment, as this tumor is indistinguishable from WT and is resistant to chemotherapy and radiation. Overall 4-year survival is between 20 and 36 months. Patients with lower stages of disease (stages I and II) have 41.8% OS, and those with high stages of disease (stages III, IV, and V) have 15.9% OS. Age also influences OS, with younger patients having worse OS than older patients. Central nervous system involvement, from a second primary tumor or dissemination of rhabdoid tumor of the kidney, is almost universally fatal. Intensive follow-up is needed for these tumors, similar to that needed for WT and RCC.

Clear Cell Sarcoma

Clear cell sarcoma of the kidney was originally described as a bone-metastasizing tumor associated with late recurrences. Peak incidence of this tumor is between 1 and 4 years of age, with a male predominance (ratio of 2:1 for male to female patients). There are no known familial or predisposition syndromes, and there are no known bilateral cases. These patients typically present with a firm palpable mass, with 15% to 60% of patients reporting pain due to skeletal metastases. Imaging findings are similar to those of WT, and clear cell sarcoma of the kidney is indistinguishable from WT on images alone.

Management is similar to that for WT, with primary radical nephrectomy and LN sampling. This is followed by radiation therapy and multidrug chemotherapy (vincristine, doxorubicin, cyclophosphamide, and etoposide). Five-year event-free survival is 75% to 85%, with 5-year OS of 85% to 90%. Despite improved survival, there is a high relapse rate within the first 3 years after treatment, especially in younger patients and those with advanced disease. With current treatment regimens, brain metastases are becoming more common than the typical bone metastases originally reported. Much like rhabdoid tumor of the kidney, these patients need to be followed up closely.

Medullary Renal Cell Carcinoma

Medullary RCC affects patients with the sickle cell trait; thus, it has a predominance in African American patients. Unfortunately, more than 90% of patients with medullary RCC typically present with advanced disease. The workup is similar to that of other renal tumors. Treatment revolves around radical nephrectomy, since the tumor is unresponsive to chemotherapy and radiation therapy. The tumor is aggressive, with almost all cases being fatal. Average survival is between 4 and 16 months after diagnosis.

Rhabdomyosarcoma

Introduction

Rhabdomyosarcoma (RMS) is a malignant soft-tissue tumor of mesenchymal origin. It is the third most common solid tumor in children and accounts for 10% to 15% of all solid pediatric tumors. The incidence

of RMS is estimated at 4.5 per million, with more than 50% of cases being diagnosed in the first decade after birth. RMS exhibits a bimodal age distribution, with the first peak between 2 and 6 years of age and the second peak between 10 and 18 years of age. Approximately 20% of RMS tumors arise in the genitourinary (GU) system and primarily involve prostate, bladder, testicular, and/or paratesticular sites. Vaginal, cervical, uterine, primary retroperitoneal, and renal RMS are other rare primary sites. The primary site of RMS is associated with prognosis, with the bladder and prostate sites considered unfavorable, and paratesticular and other GU sites considered favorable. Most cases of GU RMS are sporadic, but some have been associated with genetic syndromes such as Li-Fraumeni cancer syndrome (*p53* mutation), pleuropulmonary blastoma (*DICER1* mutation), neurofibromatosis type 1 (*NF1* mutation), Costello syndrome (*HRAS* mutation), Beckwith-Wiedemann syndrome (alteration of chromosome 11p15), and Noonan syndrome.

Multiple factors can affect the prognosis for patients with RMS. Children between 1 and 9 years of age have the best prognosis, with 5-year failure-free survival (FFS) and an OS rate of 81% and 87%, respectively. Infants younger than 1 year and children at least 10 years of age have slightly worse 5-year FFS (57% and 68%, respectively) and OS (76% for both) rates. Original tumor site (favorable vs unfavorable), tumor size (>5 cm), and resectability also affect the prognosis. Children with no residual tumor, microscopic residual tumor, and gross residual disease have 5-year OS rates of 90%, 80%, and 70%, respectively.

The 2 main histologic subtypes of RMS are embryonal and alveolar, accounting for 60% to 70% and 20% to 30% of cases, respectively, with the former having a better prognosis. Other subtypes include anaplastic, mixed, and spindle cell, but these are much rarer. Recently, genetic abnormalities consisting of a balanced translocation of gene *PAX3* (chromosome 2) or *PAX7* (chromosome 1) to *FOXO1* (chromosome 13) have been associated with a lower event-free survival of 54% and 65%, respectively. Alveolar histologic findings are associated with high rates of translocation fusion (>50%) and, thus, a worse prognosis than embryonal RMS.

Evaluation

Initial evaluation should include a full history and physical examination. GU RMS usually manifests as a large palpable mass or symptoms related to mass effect. RMS involving the bladder and/or prostate can present with hematuria, urinary retention, urgency, frequency, or palpable suprapubic mass. Paratesticular RMS appears as a painless scrotal mass at presentation, and it should be approached similarly to a primary testicular tumor through an inguinal incision. The patient should be evaluated for symptoms and signs related to the mass and metastatic disease.

Initial imaging should begin with bladder and pelvic US or testicular US (**Figure 12-3**).

US is low cost and readily available and can confirm the presence and origin of a solid mass, while also allowing assessment of surrounding structures. Formal CT of the chest, abdomen, and pelvis with IV contrast material is necessary for staging and to assess the resectability of the tumor (**Figure 12-4**).

Additional imaging may be necessary if a child presents with symptoms concerning for metastatic disease. In a young child who may require sedation to obtain good-quality images, coordinating additional imaging with other adjunct procedures (eg, biopsy, excision or resection,

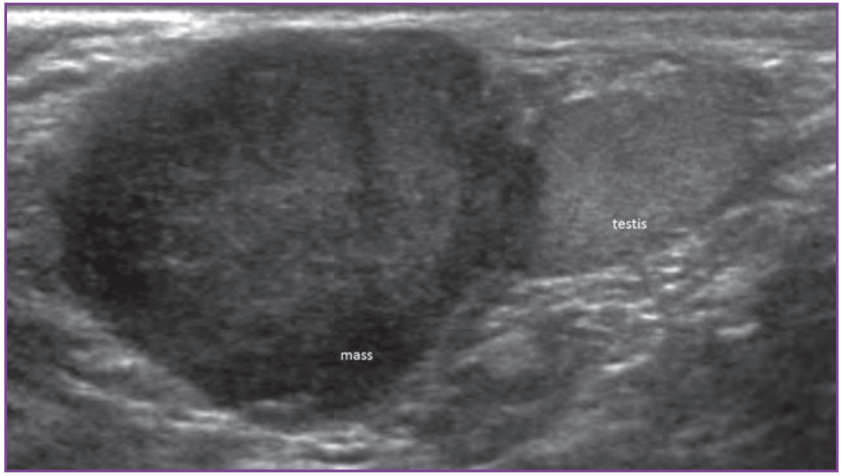

Figure 12-3. Paratesticular mass identified at scrotal ultrasonography, which turned out to be a paratesticular rhabdomyosarcoma.

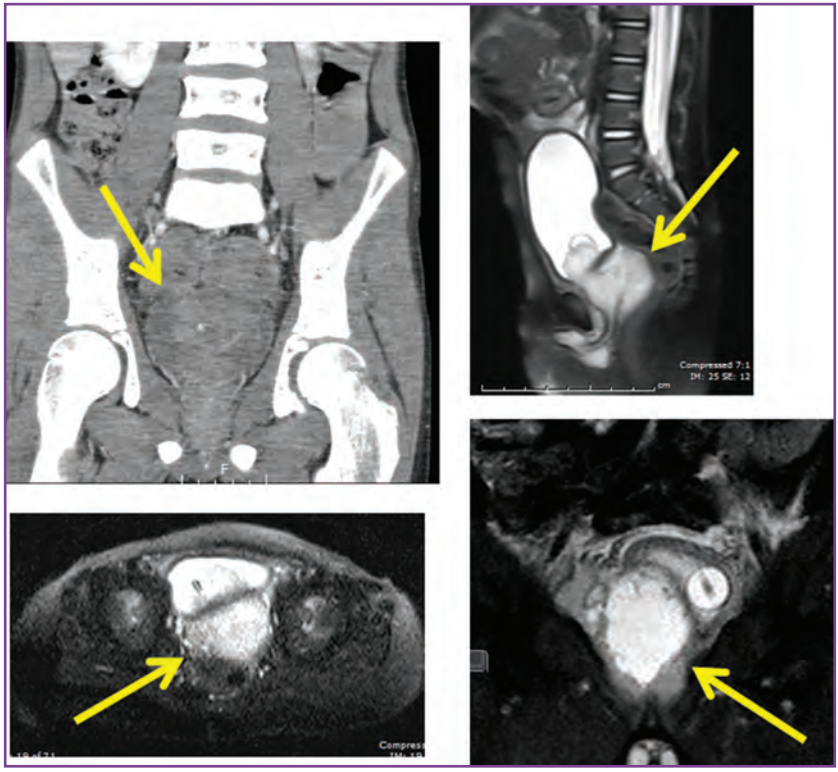

Figure 12-4. Magnetic resonance images of a large pelvic mass (arrows) displacing the bladder, which turned out to be a bladder and prostate rhabdomyosarcoma. Coronal (**A**), sagittal (**B**), and axial (**C, D**) images show the mass on different imaging planes.

vascular access placement) may be prudent. Furthermore, imaging protocols for children typically involve the use of lower doses of radiation, and it is often preferable to perform imaging at centers familiar with these protocols.

Since primary testicular tumors are more common than paratesticular tumors, testicular tumor markers (α-fetoprotein, β-human chorionic gonadotropin, and lactate dehydrogenase) should be obtained when encountered with a paratesticular tumor, particularly when the origin of the tumor is uncertain. Other studies to perform as part of the initial evaluation should include a complete blood cell count and a comprehensive metabolic panel.

Diagnosis

A formal diagnosis of GU RMS can only be established with pathologic evaluation of the tumor. In the case of paratesticular tumors, this is accomplished with radical orchiectomy. Biopsy of a paratesticular tumor is generally contraindicated. Since surgical management of other GU RMS (eg, bladder, prostate, vagina) is directed toward organ and/or function preservation, biopsy (endoscopic, percutaneous, or open) is the most common initial step toward establishing a diagnosis. However, when these tumors can be completely excised without compromising organ function, primary surgical resection is advocated. Genetic and chromosomal analysis should be performed, since these provide insights into prognosis.

Once a diagnosis is established, the tumor is assigned a stage based on the TNM classification, pathologic group, and risk group classification. Stage is assigned on the basis of the COG Soft-Tissue Sarcoma Committee by using the TNM staging system (**Tables 12-5** and **12-6**). Pathologic group classification is based on completeness or extent of initial surgical resection (**Table 12-7**) prior to the initiation of chemotherapy. Last, risk group classification is assigned on the basis of stage, pathologic group, and histologic findings (**Table 12-8**). While

Table 12-5. TNM Staging for Rhabdomyosarcoma

Stage	Findings
T1	Confined to organ of origin and no local invasion
T2	Local invasion beyond the organ of origin
a	Tumor ≤5 cm
b	Tumor ≥5 cm
N0	No clinical regional lymph node involvement
N1	Clinical regional lymph node involvement
Nx	Regional lymph nodes not examined
M0	No metastasis
M1	Metastasis present

Table 12-6. Pretreatment Stage System					
Stage	Site of Primary Tumor	T Stage	Tumor Size	N Stage	M Stage
1	Favorable	Any	Any	Any	M0
2	Unfavorable	Any	≤5 cm	N0 or Nx	M0
3	Unfavorable	Any	≤5 cm	N1	M0
			>5 cm	Any	
4	Any	Any	Any	Any	M1

Favorable sites include paratesticular, vaginal, uterine, renal, and cervical sites. Unfavorable sites include the bladder and prostate.

Table 12-7. Pathologic Group Classification	
Group	Definition
I	Localized tumor, completely removed, negative margins, and no regional lymph node involvement
II	Total gross resection with evidence of regional spread
A	Microscopic residual disease
B	Involved regional lymph node completely resected
C	Involved regional nodes resected with microscopic residual and/or involvement of most distal node
III	Localize tumor incompletely removed with gross, residual disease after biopsy or subtotal resection
IV	Distant metastases present excluding regional nodes and adjacent organs

group and stage classification are complex, they are highly predictive of prognosis. The 3-year FFS rates for pathologic groups I, II, III, and IV are 83%, 86%, 73%, and less than 30%, respectively. Similarly, 3-year FFS rates for TNM stages 1, 2, and 3 are 86%, 80%, and 68%, respectively.

Table 12-8. Rhabdomyosarcoma Risk Group Classification

Risk Group	Histologic Findings	Stage	Group
Low	Embryonal	1	I, II, III
	Alveolar	2, 3	I, II
Intermediate	Embryonal	2, 3	III
	Alveolar	1, 2, 3	I, II, III
High	Any	4	IV

Treatment

Primary surgical resection is the preferred treatment for paratesticular RMS. Contemporary treatment of GU RMS has shifted toward minimizing morbidity and reducing therapy-related toxicity. Other GU RMS are treated with biopsy and primary chemotherapy, which are then followed by surgery, radiation therapy, or both. Using this risk-stratified multimodal treatment approach has resulted in clinically significant improvement in prognosis, with expected 5-year OS rates exceeding 80%.

All children with RMS should undergo chemotherapy, with the intensity and duration dictated by the risk group designation. Children in the low-risk group (localized disease) are treated with a 2-drug (vincristine and dactinomycin) or 3-drug regimen (vincristine, dactinomycin, and cyclophosphamide [VAC]) with FFS rates of 85% to 89% and OS rates of 90% to 97%, with or without the administration of radiation therapy. Children in the intermediate-risk group are treated with VAC with OS rates of 84% to 88%. Children in the high-risk group (ie, metastatic disease) generally have poor prognosis and are treated with a more intensive chemotherapy regimen with a backbone of VAC. These patients have 5-year survival rates of up to 50%, with age younger than 1 year or at least 10 years, unfavorable primary site, bone marrow involvement, and multiple metastatic sites being the factors associated with poor prognosis. Radiation therapy is used after chemotherapy when the primary tumor is deemed unresectable, when there is residual local disease after delayed primary resection, or when there is local relapse. Radiation therapy can be omitted in patients who undergo

resection and are found to have embryonal histologic findings, localized disease, and no residual disease (low-risk group). All other groups typically undergo radiation therapy as part of their treatment. Patients who undergo delayed primary resection and have no residual disease can have reduction of radiation doses.

Surgical treatment of GU RMS includes biopsy, radical orchiectomy, prostatectomy, cystoprostatectomy, cystectomy, and partial cystectomy. Endoscopic biopsy is reserved for bladder and prostate RMS. It is performed with general anesthesia by using a cystoscope or resectoscope. When a patient is unable to accommodate the resectoscope, an open or percutaneous biopsy is performed. At the time of open biopsy, it is recommended that the regional LNs be sampled to allow better staging of the tumor. Generally, biopsy of GU RMS is associated with a low complication rate (<10%), with the most common complications consisting of infection, bleeding, or pain.

Patients with paratesticular RMS are treated with radical orchiectomy via an inguinal incision. More than 40% of patients with paratesticular RMS present with metastatic disease, with a high incidence of lymphatic spread to the retroperitoneum—particularly in children at least 10 years of age. All children 10 years and older who have paratesticular RMS require ipsilateral retroperitoneal LN dissection for staging. Retroperitoneal LN dissection can be associated with intraoperative (5%), postoperative (10%–24%), and long-term (7%) complications.

Treatment of bladder and prostate RMS is directed toward preservation of bladder function. Therefore, most patients are deemed unresectable, undergo biopsy, and then undergo chemotherapy. Most bladder and prostate RMS have pathologic group III designation. Radical cystectomy and cystoprostatectomy (anterior exenteration) with urinary diversion (ie, neobladder, continent urinary diversion, or ileal and/or colon conduit) is typically reserved for patients who have persistent biopsy-proven disease after chemotherapy and radiation therapy. Complete primary resection is no longer recommended, unless such surgery can be performed in an organ-preserving manner. After initial chemotherapy, patients can undergo delayed primary resection if complete resection is deemed feasible, and acceptable functional outcome is expected. This typically consists of partial cystectomy, which is associated with 3-year OS rates exceeding 80%. LN involvement is noted in up to 12% of patients with bladder-prostate RMS. Pelvic LN dissection is performed

primarily for staging, risk stratification, and potential reduction in radiation therapy. While bladder preservation is possible in up to 60% of patients with RMS, more than 40% of patients experience long-term bladder issues (overactivity, diminished capacity, urgency, incontinence, decrease compliance, and hemorrhagic and radiation cystitis), likely due to chemotherapy and radiation exposure.

Testis

Introduction

Primary testicular tumors in children and adolescents are rare. The estimated incidence is 0.2 to 2 per 100,000 boys. These tumors represent 1% to 2% of all pediatric solid tumors and approximately 7% of all new testicular cancer diagnoses in the United States. Testicular tumors exhibit a bimodal age distribution, with a small peak in the first 4 years after birth and a second larger peak around 15 years of age. Most testicular tumors are sporadic, and known risk factors include a history of cryptorchidism and a family history of testis cancer. Benign tumors are associated with 100% survival and no reported cases of local recurrence or metastatic disease. Malignant testicular tumors are associated with excellent prognosis, with 5-year event-free survival rates of more than 80% and 5-year OS rates between 94% and 100%.

Workup

Children and adolescents are most commonly diagnosed after a painless testicular mass is discovered (in >85% of cases) during a routine medical examination or self-examination. When a child or adolescent is found to have a testis mass, the first step is to obtain a full history and perform a physical examination. The history should be focused on identifying risk factors (eg, cryptorchidism and family history), along with signs and symptoms that may point to a hormonal issue (eg, precocious puberty) or metastatic disease (eg, flank pain, shortness of breath). The physical examination should include evaluation of the affected testicle to determine if the lesion is originating from the testis or from adjacent structures. The contralateral testis should be palpated to rule out any contralateral abnormalities. Auscultation of the lungs along with evaluation of the LNs (particularly the supraclavicular LNs) is important.

The chest should be examined to look for signs of gynecomastia, which would point toward a hormone-producing tumor of the testis. Pubertal status should be established.

Malignant germ cell tumors can produce β-human chorionic gonadotropin and α-fetoprotein, which can serve as tumor markers. Lactate dehydrogenase is a nonspecific marker of disease burden that is also measured. Tumor markers should be evaluated prior to excision of the tumor or initiation of therapy. In the setting of a testis mass and precocious puberty, a hormonal panel consisting of serum testosterone, estradiol, 17-ketosteroid level, or dexamethasone suppression testing can aid in establishing the diagnosis of a stromal tumor or congenital adrenal hyperplasia. However, delaying the referral to perform these hormonal studies is not recommended.

Initial imaging should consist of US evaluation of both testicles (**Figure 12-5**).

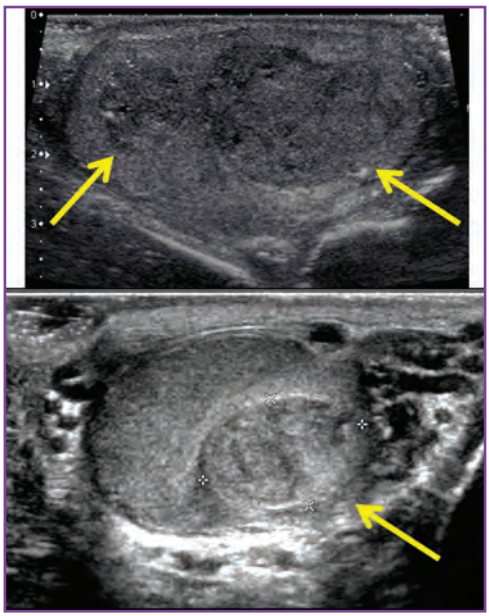

Figure 12-5. Scrotal ultrasonography shows testicular masses (arrows) in the same patient; be sure to look for multiple masses in the same testicle, as well as abnormalities in the opposite testicle.

In patients with extremely increased tumor markers or symptoms related to metastatic disease, CT of the chest, abdomen, and pelvis with oral and IV contrast material can be considered as part of the initial evaluation. However, further imaging is usually performed after a histologic diagnosis has been established. This is typically recommended in prepubertal children, who are more likely to have benign tumors and require no additional imaging. In a young child who may require sedation to obtain good-quality cross-sectional images, coordinating this at the time of tumor excision can spare the child additional anesthetic exposure and allow coordination of adjunct procedures (eg, vascular access for chemotherapy administration).

Additional Considerations

Given the excellent outcomes associated with the management of testicular tumors, there has been an increasing effort toward decreasing treatment-related morbidity. Preservation of future fertility is an important concern. In postpubertal patients, sperm banking is an easy, viable option to preserve future fertility potential. In prepubertal children, options are limited. Although still experimental, cryopreservation of testicular tissue has emerged as an option for fertility preservation in prepubertal children. Early consultation with an oncofertility specialist before the initiation of therapy (orchiectomy or chemotherapy) can help guide patients and parents through this process.

Diagnosis

Benign and malignant testicular neoplasms can be encountered at any age. Pubertal status, US findings, and serum tumor markers can help narrow the differential diagnosis. However, a formal diagnosis can only be established with pathologic evaluation of the completely excised tumor. Biopsy of a testis tumor without complete excision is contraindicated. Common histologic findings for testis tumors in children and adolescents include germ cell tumors (yolk sac, embryonal, choriocarcinoma, and teratoma), epidermoid cyst, stromal tumors (Leydig cell tumors, Sertoli cell tumors, and juvenile granulosa cell tumors), adrenal rest (associated with congenital adrenal hyperplasia), and gonadoblastoma (usually observed in patients with disorders of sexual development). Seminoma, although a germ cell tumor, is rarely observed in children and adolescents.

Leukemia and lymphoma are the most common metastatic lesions of the testes, and these should be considered as part of the differential diagnosis with bilateral tumors. Tumors appearing as a scrotal mass at presentation could be paratesticular in origin. These rare tumors can be benign or malignant. Common benign paratesticular tumors include leiomyoma, fibroma, lipoma, cystadenoma, adenomatoid tumor, and hemangioma. Malignant paratesticular tumors include leiomyosarcoma, fibrosarcoma, liposarcoma, and RMS. Of the paratesticular tumors, RMS is the most common and accounts for 40% of paratesticular tumors. Testicular and paratesticular tumors are generally treated in the same fashion.

More than 70% of prepubertal tumors are benign, and malignant prepubertal tumors tend to be less aggressive than their postpubertal counterparts. The most common malignant prepubertal tumors are mature teratoma and yolk sac. In prepubertal children, mature teratoma is typically localized and rarely metastatic. Most yolk sac tumors manifest with localized disease (>70% of cases), but approximately 20% of patients can experience relapse.

Most postpubertal tumors are malignant germ cell tumors (yolk sac tumor, embryonal tumor, choriocarcinoma, and teratoma). Embryonal tumor is the most common tumor, but it is often metastatic at the time of diagnosis. Teratoma is rarely found alone and is often found in conjunction with other germ cell tumors. Intratubular germ cell neoplasia is a known precursor of testicular cancer in adults and is often found in association with postpubertal tumors but not prepubertal tumors.

Treatment

Initial treatment of testis tumors involves radical orchiectomy or testicular-sparing surgery (TSS), also known as *partial orchiectomy.* Both of these procedures are performed via an inguinal incision and are typically performed as outpatient surgeries. These procedures are associated with minimal discomfort and rapid postoperative recovery. Overall complication rates for these procedures are low, with most common complications consisting of hematoma and wound infection.

Radical orchiectomy remains the standard of reference for the treatment of most testicular tumors. It provides local tumor control and histologic diagnosis, along with information used for tumor staging and risk stratification. This involves complete removal of the testicle and spermatic

cord at the level of the internal inguinal ring. Since the entire testicle is removed, a testicular prosthesis is an option if the parents and child so desire. A testicular prosthesis can be placed at the time of orchiectomy or deferred to a later time, particularly in the young child, whose other testicle may not have reached its full size.

Given the high rate of benign tumors (>70%) in prepubertal boys, TSS has played an increasing role in the treatment of testis tumors, particularly for tumors smaller than 2.5 cm. TSS is approached similarly to radical orchiectomy, but with the goal of only removing the tumor and sparing the surrounding, uninvolved testicular tissue. Intraoperative frozen section is used during TSS to establish a histologic diagnosis. If a malignant tumor or indeterminate diagnosis is encountered, completion orchiectomy is immediately performed. The use of TSS in postpubertal tumors remains controversial and is typically used in special circumstances, such as synchronous bilateral testicular tumors, metachronous contralateral tumors, lesions in a solitary testis, or when a benign tumor is suspected (normal tumor markers, benign appearance at US). TSS should only be attempted when the entire tumor can be safely removed, when there is access to intraoperative frozen pathologic sampling, when enough uninvolved testicular tissue can be preserved, and, most importantly, when oncologic local control is not compromised. Much like radical orchiectomy, TSS is associated with a low complication rate, with complications specific to TSS consisting of testicular atrophy and/or loss (<5% of cases), hematoma (2% of cases), and infection (1% of cases). **Figure 12-6** shows preoperative images in a prepubertal patient treated with TSS, with pathologic images of all 3 germ cell layers.

Benign tumors typically require no further imaging or therapies after they have been completely excised. Stromal tumors treated with TSS in postpubertal adolescents have excellent results, with no observed metastasis or death, and only a 3% rate of local recurrence, which can be salvaged with completion orchiectomy. Additional therapies for malignant tumors are based on histologic diagnosis and stage. Staging for testis tumors is based on a combination of cross-sectional imaging, pathologic stage, and postoperative tumor markers. Tumor markers should be checked after at least 4 half-lives (approximately 8 days for β-human chorionic gonadotropin, 12 days for lactate dehydrogenase, and 20 days for α-fetoprotein) to ensure normalization (**Table 12-9**).

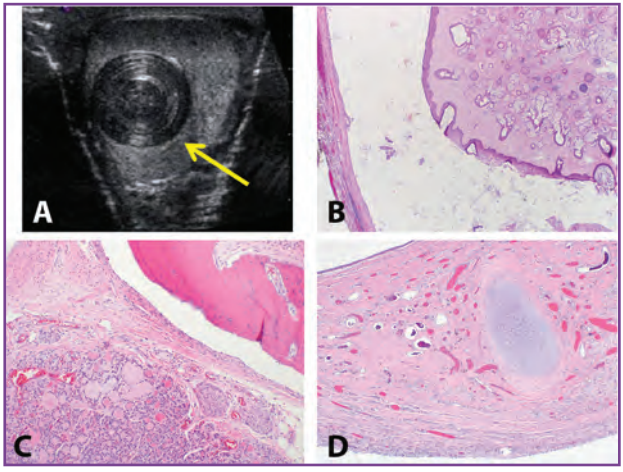

Figure 12-6. Prepubertal teratoma in a prepubertal male patient. **A,** Preoperative ultrasonography shows the classic "onion-skin" appearance of a suspected teratoma (arrow). **B,** Photomicrograph (hematoxylin-eosin stain; original magnification, ×4) shows the skin and adnexal structures. **C,** Photomicrograph (hematoxylin-eosin stain; original magnification, ×4) shows the bone and thyroid tissue. **D,** Photomicrograph (hematoxylin-eosin stain; original magnification, ×4) shows the cartilage and fibrovascular tissue.

Table 12-9. Tumor Marker Level Classification

Stage	Human Chorionic Gonadotropin Level (Half-life of 1–3 d)	Lactate Dehydrogenase Level (Half-life of 4–5 d)	αFetoprotein Level (Half-life of 5–7 d)
S0	Normal	Normal	Normal
S1	<5,000	<1.5 × normal	<1,000
S2	5,000–50,000	1.5–10 × normal	1,000–10,000
S3	>50,000	>10 × normal	>10,000
Sx	Markers not available		

Note that normal levels for tumor markers vary between laboratories.

Tumors in prepubertal and young postpubertal children are staged and treated per current COG protocols (**Table 12-10**).

Adolescents are typically staged per the American Joint Committee on Cancer *Cancer Staging Manual,* 7th Edition, which is based on the Union for International Cancer Control TNM system, in conjunction with the International Germ Cell Cancer Collaborative Group risk stratification if they have metastatic disease (**Tables 12-11** and **12-12**).

Therapy for these patients is based on the established National Comprehensive Cancer Network guidelines on the treatment of testicular tumors. Patients with localized disease are typically treated with orchiectomy, followed by surveillance, even when high-risk features are present (ie, lymphovascular invasion and embryonal carcinoma), since recurrence in these patients can be invariably salvaged with chemotherapy. In patients with metastatic disease, chemotherapy is usually first-line treatment, with retroperitoneal LN dissection playing a minor role and radiation therapy reserved for seminoma. Overall, prognosis for children and adolescents with testicular malignancy is good, and an OS rate between 94% and 100% is expected. Patients with a diagnosis of malignant testicular tumor require lifelong follow-up that consists of imaging of the retroperitoneum and lungs and physical examination of the contralateral testis.

Table 12-10. Children's Oncology Group Testicular Tumor Stages

Stage	Definition
I	Limited to the testis, completely resected, and normal tumor marker levels
II	Tumor removed via a scrotal approach; tumor spillage; microscopic residual disease; or increased tumor markers
III	Gross residual disease with involvement of the retroperitoneal lymph nodes
IV	Metastatic disease beyond the retroperitoneum (liver, brain, bone, and lung)

Table 12-11. TNM Staging System	
Primary Tumor (T): Extent Classified After Radical Orchiectomy	
pTX	Primary tumor cannot be assessed.
pT0	No residual tumor
pTis	Intratubular germ cell neoplasia
pT1	Tumor limited to the testis and epididymis and no vascular or lymphatic invasion; tumor may invade into the tunica albuginea but not the tunica vaginalis.
pT2	Tumor limited to the testis and epididymis with vascular or lymphatic invasion, or tumor extending through the tunica albuginea with involvement of the tunica vaginalis
pT3	Tumor invades the spermatic cord.
pT4	Tumor invades the scrotum.
Regional Lymph Nodes: Clinical Stage Based on Imaging Findings	
NX	Regional lymph nodes cannot be assessed.
N0	No regional lymph node metastasis
N1	Lymph node mass ≤2 cm in greatest dimension or multiple lymph nodes, none >2 cm in the greatest dimension
N2	Lymph node mass >2 cm but <5 cm in the greatest dimension or multiple lymph nodes, any one mass >2 cm but <5 cm in the greatest dimension
N3	Metastasis with a lymph node mass >5 cm in the greatest dimension
Regional Lymph Nodes[a]: Pathologic Stage Based on Lymph Node Analysis	
pNX	Regional lymph nodes cannot be assessed.
pN0	No regional lymph node metastasis

Continued

Table 12-11 (*continued*)

Regional Lymph Nodes[a]: Pathologic Stage Based on Lymph Node Analysis (*continued*)			
pN1	Metastasis to lymph node with mass ≤2 cm in the greatest dimension or ≤5 nodes with positive findings, none >2 cm in the greatest dimension		
pN2	Metastasis to lymph node mass >2 cm but not >5 cm in the greatest dimension, or >5 nodes with positive findings, none >5 cm, or evidence of extranodal extension of tumor		
pN3	Metastasis to lymph node mass >5 cm in the greatest dimension		
Metastasis (M)			
M0	No distant metastasis		
M1	Distant metastasis	M1a	Nonregional nodal or pulmonary metastasis
		M1b	Distant metastasis other than to nonregional nodes and lungs

[a] Regional nodes include abdominal nodes that are preaortic, para-aortic, retroaortic, interaortocaval, precaval, paracaval, retrocaval, and along the spermatic vein.

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Bladder

Introduction

Bladder tumors commonly found in children are presented in **Table 12-13**.

There are limited data on urothelial cell carcinoma of the bladder (UCCb) in the pediatric population, consisting mostly of case reports and small case series. In a Surveillance, Epidemiology, and End Results (SEER) Program database review from 1973 to 2003, 140 bladder malignancies were found in patients younger than 18 years in the United States. This is a rare diagnosis in children and is much more commonly seen in older patients who have a long history of smoking

Table 12-12. Testicular Tumor Stage Grouping

Stage	Tumor Stage Grouping	Primary Tumor	Nodes	Metastasis	Serum Tumor Markers
Stage 0		pTis	N0	M0	S0
Stage I	I	pT1-4	N0	M0	Sx
	IA	pT1			S0
	IB	pT2-4			
	IS	Any pT			S1-3
Stage II	II	Any pT	N1-3	M0	Sx
	IIA		N1		S0-1
	IIB		N2		
	IIC		N3		
Stage III	III	Any pT	Any N	M1	SX
	IIIA			M1a	S0-1
	IIIB			M0-M1a	S2
	IIIC			Any M	S3

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or other occupational exposures. In children, these tumors are typically low grade and low stage and recur infrequently. Fewer than 7 cases of high-grade UCCb in patients younger than 18 years have been reported in the literature, with some authors suggesting that pediatric UCCb be considered a completely different disease from the adult form. Grade, in addition to stage, dictates treatment and prognosis.

UCCb has been reported in 0.1% to 0.4% of the population younger than 20 years, with fewer than 35 cases in patients younger than

Table 12-13. Common Bladder Tumors in Children

Tumor Type	Features	Follow-up
Papilloma	Benign; may recur; never progresses	No follow-up needed
Papillary urothelial neoplasm of low malignant potential	May recur; rarely progresses	Consider similar to low-grade urothelial cell carcinoma of the bladder
Nephrogenic-adenoma	Benign; inflammatory; reactive; commonly associated with urinary tract infection	Complete resection, antibiotics administered for 1 year, no follow-up needed
Fibroepithelial polyp	Benign	No follow-up needed
Inflammatory myofibroblastic tumor	Indeterminate; may recur	4%–20% recurrence rate in adults (no recurrence confirmed in children), usually followed with serial ultrasonography and cystoscopy
Leiomyoma	Benign	No follow-up needed
Leiomyosarcoma	Malignant; usually history of retinoblastoma or cyclophosphamide therapy	Consult oncology
Cystitis glandularis	Benign; inflammatory; reactive	Risk of adenocarcinoma in adults, unknown in children
Adenocarcinoma	Malignant; associated with urachal remnant	Consult oncology; partial cystectomy
Rhabdomyosarcoma	See the Rhabdomyosarcoma section of this chapter.	

10 years. In the pediatric population, UCCb occurs most commonly in male patients and is seen more often in the white population. In patients younger than 12 years, bladder tumors are more likely to represent RMS, with UCCb becoming the predominant histologic finding around puberty. The median age of diagnosis for UCCb is between 11 and 12 years, and that diagnosis is often delayed up to 25 months after symptom onset.

The tumor is typically located at the trigone and is solitary. Unlike in adults, these tumors have a low recurrence rate; the recurrence rate is 40% to 70% in adults but only about 13% in children. Most cases are low grade and superficial.

The etiologic origins of adult bladder cancer are well described and include smoking, radiation exposure, chemicals, and occupational exposures. These factors are much less likely to contribute to pediatric bladder cancer, given the much earlier age of onset and minimal, if any, exposure to these substances. The early onset of UCCb in pediatric patients suggests a possible genetic predisposition. Familial clustering has been reported to double the risk, but investigators have not been able to eliminate possible shared environmental factors.

There have been reports of UCCb developing in patients with retinoblastoma (irrespective of radiotherapy exposure), Costello syndrome, Alport syndrome, and Turner syndrome. While upper-tract urothelial cell carcinoma has been linked with various syndromes, there is insufficient evidence to determine the influence of Lynch syndrome (hereditary nonpolyposis colorectal cancer) on UCCb. Analysis of pathologic specimens shows that genetic and epigenetic alterations linked to adult UCCb are extremely rare in pediatric patients.

Because of the rarity of this condition, normal presentation is difficult to elucidate in the literature. Persistent, painless gross hematuria is the most common symptom and has been reported in multiple series. Other symptoms that have been reported include irritative voiding and pain. Delayed diagnosis is common, occurring in up to 25% of patients.

Workup

A thorough history and physical examination are necessary, focusing on the family history and the potential environmental or genetic risk factors. Urinalysis, urine culture, and renal and bladder US are typical

of the initial workup. US (**Figure 12-7**) is very sensitive in the detection of bladder tumors in children. Bladder tumors as small as 5 mm can be seen as papillary lesions at US. When US indicates a bladder tumor, or when there is no other cause of the hematuria, cystoscopy is the next step in diagnosis.

A tissue diagnosis is important in establishing a diagnosis of UCCb. This is usually established by resecting the tumor with a transurethral approach. It is important that the pathologist reports the grade of the tumor as well as the depth of invasion, since both of these factors influence how the tumor is treated. Identification of muscle in the specimen is important; if muscle is not present, a repeat biopsy is mandatory, particularly for malignant tumors.

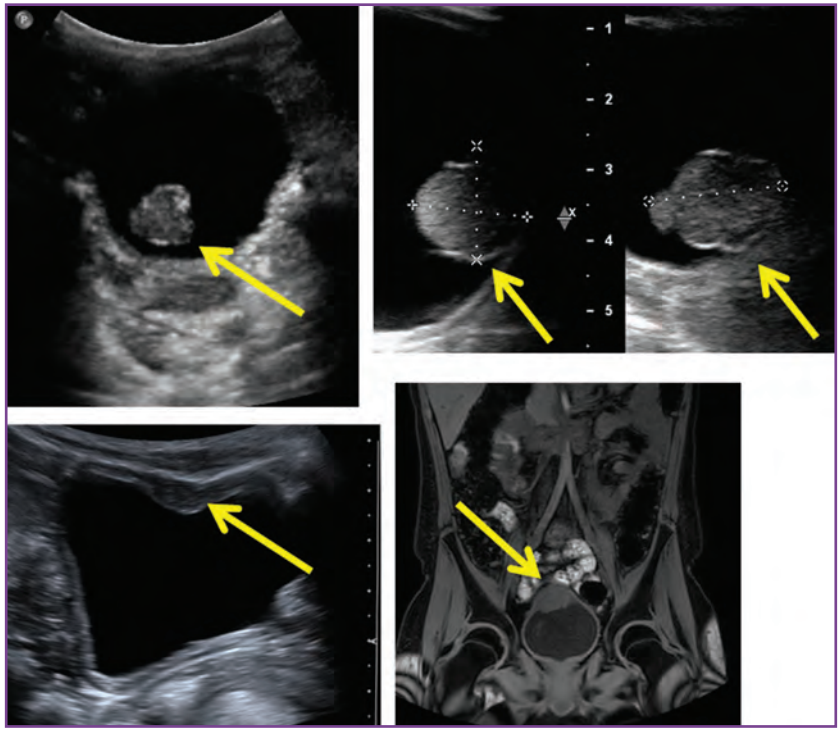

Figure 12-7. Various bladder masses (arrows) as depicted with ultrasonography (**A, B, C**) and coronal magnetic resonance imaging (**D**).

Diagnosis

Because of the low recurrence rate when compared with adults, these lesions typically do not need much further management beyond complete initial resection. On the basis of the pathology report, however, repeat resection and possibly intravesical therapy may be used if high-grade histologic findings are identified.

In adults, a single intravesical dose of chemotherapy (typically mitomycin C) is administered immediately after transurethral resection. In children, this has been used, but there are no specific guidelines to support routine use.

These tumors are typically isolated and treated completely with transurethral resection. The 5-year survival rate for UCCb has been reported at 97.3%, indicating an excellent prognosis. The longest interval to recurrence reported in the literature is 7.5 years, with multiple investigators reporting no recurrences at a median follow-up of 5 years.

While recurrence of UCCb is rare, in patients up to 20 years of age, the risk of recurrence, progression, and death is 3.4%, 1.1%, and 1.1%, respectively. Progression and death are likely caused by rare cases of high-grade and invasive tumors. If a low-grade UCCb recurs, it is usually a papilloma or papillary urothelial neoplasm of low malignant potential, both of which have no risk of metastasis and excellent outcomes after resection.

The intensity of follow-up should be proportional to the risk of disease recurrence or progression. Unfortunately, there are few data on the natural history of UCCb in children; thus, follow-up protocols vary widely. Unlike in adult patients, the role of upper-tract imaging and cytology in children is not well defined. Upper-tract imaging exposes children to clinically significant amounts of radiation. Urine cytology for low-grade tumors has a reported sensitivity under 40%; thus, the routine use of cytology to detect low-grade UCCb, which is most common in children, is limited. While considered the standard of reference, frequent cystoscopic evaluation exposes children to multiple anesthetics, which is not without risk. Follow-up with bladder US seems reasonable.

When to Refer

- Refer a patient with any palpable testicular or paratesticular mass to a pediatric urologist and oncofertility specialist immediately (don't wait for US or tumor marker results).
- Refer a patient to a pediatric urologist as soon as possible when there are any atypical US findings concerning for a tumor of the bladder, kidneys, or adrenal glands.

Clinical Pearls

- Every effort should be made to minimize the time from initial presentation to initiation of definitive therapy.
- Cross-sectional imaging for all suspected urological malignancies should be directed by a multidisciplinary oncology team by using pediatric protocols to minimize radiation exposure and performing imaging in combination with other procedures to reduce exposure to anesthetic.
- Initial workup for a renal mass should include abdominal US, complete blood cell count, urinalysis, comprehensive metabolic panel, and coagulation studies.
- Age can help in establishing the likely diagnosis of a renal mass (CMN in an infant younger than 6 months, WT in a child younger than 12 years, and RCC in an adolescent older than 12 years).
- Pediatric RCC is associated with advanced disease at presentation, regardless of the size of the mass.
- Paratesticular RMS should be managed with primary resection, similar to testicular tumors.
- Children at least 10 years of age who have paratesticular RMS should undergo ipsilateral retroperitoneal LN dissection after primary tumor resection for staging.
- Contemporary treatment of bladder and prostate RMS generally consists of biopsy to establish the diagnosis and primary chemotherapy, followed by surgery, radiation therapy, or both, with the goal of bladder preservation.
- A newly discovered testicular mass should be evaluated with a history and physical examination, and referral to a pediatric urologist and oncofertility specialist should be initiated immediately.

- Initial imaging and laboratory studies for a testicular or scrotal mass should be limited to testicular US and tumor markers (β-human chorionic gonadotropin, α-fetoprotein, and lactate dehydrogenase).
- Most prepubertal testicular tumors are benign, and malignant tumors tend to be localized and associated with excellent prognosis.
- Although most postpubertal testicular tumors are malignant, these are associated with excellent prognosis, even when metastatic.
- Patients with testicular tumors require long-term follow-up to detect and treat disease relapse.
- Bladder tumors are rare in the pediatric population and require resection to establish a diagnosis.

Resources for Parents

- Children's Oncology Group. Wilms tumor and other kidney cancers. https://childrensoncologygroup.org/index.php/wilmstumorandotherkidneycancers. Updated July 2011. Accessed October 17, 2018
- Children's Oncology Group. Rhabdomyosarcoma. https://childrensoncologygroup.org/index.php/rhabdomyosarcoma. Updated July 2011. Accessed October 17, 2018
- Children's Oncology Group. Just diagnosed. https://childrensoncologygroup.org/index.php/newly-diagnosed-with-germ-cell-tumors. Updated September 2011. Accessed October 17, 2018
- KidsHealth. Wilms tumor. http://kidshealth.org/en/parents/wilms.html. Reviewed August 2016. Accessed October 17, 2018
- KidsHealth. Rhabdomyosarcoma (RMS). http://kidshealth.org/en/parents/rms.html. Reviewed September 2016. Accessed October 17, 2018
- American Cancer Society. Wilms tumor. https://www.cancer.org/cancer/wilms-tumor.html. Accessed October 17, 2018
- American Cancer Society. Rhabdomyosarcoma. https://www.cancer.org/cancer/rhabdomyosarcoma.html. Accessed October 17, 2018
- National Cancer Institute. Wilms tumor and other childhood kidney tumors treatment (PDQ)—patient version. https://www.cancer.gov/types/kidney/patient/wilms-treatment-pdq. Updated July 9, 2018. Accessed October 17, 2018

- National Cancer Institute. Childhood rhabdomyosarcoma treatment (PDQ)—patient version. https://www.cancer.gov/types/soft-tissue-sarcoma/patient/rhabdomyosarcoma-treatment-pdq. Updated April 30, 2018. Accessed October 17, 2018
- National Cancer Institute. Testicular cancer—patient version. https://www.cancer.gov/types/testicular. Accessed October 17, 2018
- National Cancer Institute. Unusual cancers of the reproductive and urinary systems. https://www.cancer.gov/types/childhood-cancers/patient/unusual-cancers-childhood-pdq#section/_64. Updated July 9, 2018. Accessed October 17, 2018
- National Cancer Institute. Adolescents and young adults with cancer. https://www.cancer.gov/types/aya. Reviewed January 31, 2018. Accessed October 17, 2018
- Testicular Cancer Society. http://www.testicularcancersociety.org. Accessed October 17, 2018

Suggested Readings

Kidney

Green DM. The evolution of treatment for Wilms tumor. *J Pediatr Surg*. 2013;48(1):14–19

England RJ, Haider N, Vujanic GM, et al. Mesoblastic nephroma: a report of the United Kingdom Children's Cancer and Leukaemia Group (CCLG). *Pediatr Blood Cancer*. 2011;56(5):744–748

Geller JI, Ehrlich PF, Cost NG, et al. Characterization of adolescent and pediatric renal cell carcinoma: a report from the Children's Oncology Group study AREN03B2. *Cancer*. 2015;121(14):2457–2464

Tomlinson GE, Breslow NE, Dome J, et al. Rhabdoid tumor of the kidney in the National Wilms' Tumor Study: age at diagnosis as a prognostic factor. *J Clin Oncol*. 2005;23(30):7641–7645

Seibel NL, Sun J, Anderson JR, et al. Outcome of clear cell sarcoma of the kidney (CCSK) treated on the National Wilms Tumor Study-5 (NWTS). *J Clin Oncol*. 2006;24(18 Suppl):9000

Rhabdomyosarcoma

Dasgupta R, Rodeberg DA. Update on rhabdomyosarcoma. *Semin Pediatr Surg*. 2012;21(1):8–78

Perez EA, Kassira N, Cheung MC, Koniaris LG, Neville HL, Sola JE. Rhabdomyosarcoma in children: a SEER population based study. *J Surg Res*. 2011;170(2):e243–e251

Dehner LP, Jarzembowski JA, Hill DA. Embryonal rhabdomyosarcoma of the uterine cervix: a report of 14 cases and a discussion of its unusual clinicopathological associations. *Mod Pathol*. 2012;25(4):602–614

Ferrari A, Bisogno G, Macaluso A, et al. Soft-tissue sarcomas in children and adolescents with neurofibromatosis type 1. *Cancer*. 2007;109(7):1406–1412

Crucis A, Richer W, Brugières L, et al. Rhabdomyosarcomas in children with neurofibromatosis type I: a national historical cohort. *Pediatr Blood Cancer*. 2015;62(10):1733–1738

Malempati S, Rodeberg DA, Donaldson SS, et al. Rhabdomyosarcoma in infants younger than 1 year: a report from the Children's Oncology Group. *Cancer*. 2011;117(15):3493–3501

Crist W, Gehan EA, Ragab AH, et al. The Third Intergroup Rhabdomyosarcoma Study. *J Clin Oncol*. 1995;13(3):610–630

Smith LM, Anderson JR, Qualman SJ, et al. Which patients with microscopic disease and rhabdomyosarcoma experience relapse after therapy? A report from the soft tissue sarcoma committee of the children's oncology group. *J Clin Oncol*. 2001;19(20):4058–4064

Parham DM, Ellison DA. Rhabdomyosarcomas in adults and children: an update. *Arch Pathol Lab Med*. 2006;130(10):1454–1465

Crist WM, Anderson JR, Meza JL, et al. Intergroup rhabdomyosarcoma study-IV: results for patients with nonmetastatic disease. *J Clin Oncol*. 2001;19(12):3091–3102

Raney B, Anderson J, Jenney M, et al; Children's Oncology Group Soft-Tissue Sarcoma Committee; International Society of Pediatric Oncology Malignant Mesenchymal Tumors Group; German Cooperative Weichteilsarkomstudie Group; Italian Soft-Tissue Sarcoma Cooperative Group. Late effects in 164 patients with rhabdomyosarcoma of the bladder/prostate region: a report from the international workshop. *J Urol*. 2006;176(5):2190–2194, discussion 2194–2195

Breneman JC, Lyden E, Pappo AS, et al. Prognostic factors and clinical outcomes in children and adolescents with metastatic rhabdomyosarcoma—a report from the Intergroup Rhabdomyosarcoma Study IV. *J Clin Oncol*. 2003;21(1):78–84

Rodeberg D, Arndt C, Breneman J, et al. Characteristics and outcomes of rhabdomyosarcoma patients with isolated lung metastases from IRS-IV. *J Pediatr Surg*. 2005;40(1):256–262

Seitz G, Dantonello TM, Int-Veen C, et al; CWS-96 Study Group. Treatment efficiency, outcome and surgical treatment problems in patients suffering from localized embryonal bladder/prostate rhabdomyosarcoma: a report from the Cooperative Soft Tissue Sarcoma trial CWS-96. *Pediatr Blood Cancer*. 2011;56(5):718–724

Ahmed HU, Arya M, Muneer A, Mushtaq I, Sebire NJ. Testicular and paratesticular tumours in the prepubertal population. *Lancet Oncol*. 2010;11(5):476–483

Rodeberg DA, Paidas CN, Lobe TL, et al. Surgical principles for children/adolescents with newly diagnosed rhabdomyosarcoma: a report from the soft tissue sarcoma committee of the Children's Oncology Group. *Sarcoma*. 2002;6(4):111–122

Testis

Walsh TJ, Grady RW, Porter MP, Lin DW, Weiss NS. Incidence of testicular germ cell cancers in U.S. children: SEER program experience 1973 to 2000. *Urology*. 2006;68(2): 402–405, discussion 405

American Cancer Society. Key statistics for testicular cancer. https://www.cancer.org/cancer/testicular-cancer/about/key-statistics.html. Revised May 17, 2018. Accessed October 17, 2018

Grantham EC, Caldwell BT, Cost NG. Current urologic care for testicular germ cell tumors in pediatric and adolescent patients. *Urol Oncol*. 2016;34(2):65–75

Rescorla FJ, Ross JH, Billmire DF, et al. Surveillance after initial surgery for stage I pediatric and adolescent boys with malignant testicular germ cell tumors: report from the Children's Oncology Group. *J Pediatr Surg*. 2015;50(6):1000–1003

Amini A, Waxweiler TV, Maroni PD, et al. Survival outcomes of adolescent and adult patients with non-seminomatous testicular germ-cell tumors: a population-based study. *J Pediatr Urol*. 2016;12(6):405.e1–405.e9

Akiyama S, Ito K, Kim WJ, Tanaka Y, Yamazaki Y. Prepubertal testicular tumors: a single-center experience of 44 years. *J Pediatr Surg*. 2016;51(8):1351–1354

Onofre J, Baert Y, Faes K, Goossens E. Cryopreservation of testicular tissue or testicular cell suspensions: a pivotal step in fertility preservation. *Hum Reprod Update*. 2016;22(6): 744–761

Cost NG, Lubahn JD, Adibi M, et al. A comparison of pediatric, adolescent, and adult testicular germ cell malignancy. *Pediatr Blood Cancer*. 2014;61(3):446–451

Giannarini G, Dieckmann KP, Albers P, Heidenreich A, Pizzocaro G. Organ-sparing surgery for adult testicular tumours: a systematic review of the literature. *Eur Urol*. 2010;57(5):780–790

Gentile G, Brunocilla E, Franceschelli A, et al. Can testis-sparing surgery for small testicular masses be considered a valid alternative to radical orchiectomy? A prospective single-center study. *Clin Genitourin Cancer*. 2013;11(4):522–526

Ates F, Malkoc E, Zor M, et al. Testis-sparing surgery in small testicular masses not suspected to be malignant. *Clin Genitourin Cancer*. 2016;14(1):e49–e53

Edge SB, Compton CC. The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol*. 2010;17(6): 1471–1474

National Comprehensive Cancer Network. About the NCCN clinical practice guidelines in oncology. https://www.nccn.org/professionals/default.aspx. Accessed October 17, 2018

Cost NG, Lubahn JD, Adibi M, et al. Risk stratification of pubertal children and post-pubertal adolescents with clinical stage I testicular nonseminomatous germ cell tumors. *J Urol*. 2014;191(5 Suppl):1485–1490

Bladder

Alanee S, Shukla AR. Bladder malignancies in children aged <18 years: results from the Surveillance, Epidemiology and End Results database. *BJU Int*. 2010;106(4):557–560

Berrettini A, Castagnetti M, Salerno A, et al. Bladder urothelial neoplasms in pediatric age: experience at three tertiary centers. *J Pediatr Urol*. 2015;11(1):26.e1–26.e5

Ander H, Dönmez Mİ, Yitgin Y, et al. Urothelial carcinoma of the urinary bladder in pediatric patients: a long-term follow-up. *Int Urol Nephrol*. 2015;47(5):771–774

Caione P, Patruno G, Pagliarulo V, et al. Nonmuscular invasive urothelial carcinoma of the bladder in pediatric and young adult patients: age-related outcomes. *Urology*. 2017;99:215–220

CHAPTER 13

Neurogenic Bladder

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Introduction

Neurogenic bladder results from congenital or acquired dysfunction of the spinal cord or peripheral nerves to the bladder. This condition may lead to failure to adequately store and/or empty urine at safe pressures and to potentially cause clinically significant renal morbidity.

Spina bifida (SB) is the most common cause of congenital neuromuscular dysfunction in the pediatric population. Other congenital etiologic origins of neurogenic bladder include anorectal malformations and sacral agenesis, while acquired etiologic origins include spinal cord injury, spinal cord tumors, extensive pelvic surgery, and developmental issues, such as Down syndrome or cerebral palsy. Idiopathic neurogenic bladder is also encountered and may appear with chronic urinary retention or incontinence at presentation (**Box 13-1**).

This chapter will focus on SB and spinal cord injury, since both contribute to most cases of pediatric neurogenic bladder.

The diagnosis and management of neurogenic bladder has evolved over the past half-century. Prior to the 1960s, patients with neurogenic bladder had a 40% to 90% risk of upper tract deterioration by 10 years of age, and renal failure was the leading cause of death in patients with SB who survived the first 2 years. With advancements in neurosurgical and

Box 13-1. Congenital and Acquired Causes for Neurogenic Bladder

Congenital Causes	Acquired Causes
Myelomeningocele Closed and occult forms of neural tube defects Sacral agenesis Anorectal malformations	Spinal cord injury or lesion Cerebral palsy Brain tumor or lesions Pelvic surgery Idiopathic causes

urological management, most patients, with proper management and follow-up, will live into adulthood with minimal renal sequelae.

Epidemiology of Spina Bifida and Other Neural Tube Defects

SB is a neural tube defect (NTD) and the most common nonchromosomal birth defect, with an incidence of 3.1 per 10,000 births in the United States. Approximately 1,500 children are born with SB in the United States annually, with a decreasing incidence over the past 2 decades. Latino children in the United States have the highest incidence rate, at 4.2 per 10,000 births. In less developed countries, this rate can be 20-fold higher. Neurogenic bladder is present in more than 90% of cases of myelomeningocele (MMC), which is the most common and severe form of SB. Neurogenic bladder is less common in less severe forms of SB.

Low levels of folic acid or impairment in folate-mediated pathways in pregnant women is a major risk factor for NTD. In 1992, the U.S. Public Health Service recommended that all women of childbearing age consume 400 mcg of folic acid daily to reduce the risk of having a pregnancy affected by NTD. The U.S. Food and Drug Administration (FDA) mandated that folic acid be added to all enriched grains in 1996, and this has led to an estimated 28% reduction in NTD. Adequate levels of folic acid are necessary during the first few weeks of pregnancy as the neural tube is developing; therefore, it is recommended that women begin supplementation at a minimum of 2 months prior to becoming pregnant. Other risk factors that have been implicated in NTD include maternal obesity, diabetes, and young and advanced maternal age.

Pathophysiology

The neural tube develops around the 18th day of gestation. Closure occurs in the cephalad to caudal direction, should be complete by 35 days, and involves folic acid—hence the necessity of having adequate folic acid stores early in the pregnancy.

NTD may result in abnormal development of the spinal cord or vertebral structures (also termed *myelodysplasia*). Open NTD (MMC) presents as a spectrum, and the degree of resulting neural maldevelopment and trauma to exposed neural elements determine the severity of neuropathy. MMC can occur at any level of the spinal cord, with the most common being lumbar or sacral. Closed NTDs, such as meningocele, lipomeningocele, and tethered cord, can also result in neurogenic bladder.

Bladder dysfunction, as well as bowel and sexual dysfunction, are common in SB because the end organs receive nerves that emanate from the areas of the lumbar and sacral spinal cord that are usually affected by SB. Interestingly, the level of the lesion or the type of lesion does not often correlate with severity of disease, bladder dysfunction, or overall prognosis. **Figure 13-1** illustrates the innervation of the bladder-sphincter complex.

The hypogastric nerve provides afferent sympathetic innervation to the bladder, bladder neck, and urethra from the lumbar spinal cord. Sacral nerve roots provide motor, sensory, and parasympathetic innervation to the bladder and bladder neck, via the pelvic nerve. Somatic innervations of the striated urinary (and anal) sphincters also travel from sacral dorsal nerve roots via the pudendal nerve. As a result, any one of these neural elements can be impaired, causing sequelae of neurogenic bladder with impaired storage and/or emptying of urine. Lower urinary tract symptoms of neurogenic bladder vary but can include urinary incontinence, incomplete emptying, and recurrent urinary tract infections (UTIs). Patients can have "hostile" bladders with decreased capacity and/or increased bladder storage pressures that put the upper urinary tract at risk for nephropathy. Hydronephrosis may be a sign of poor bladder compliance or incomplete emptying. Secondary vesicoureteral reflux (VUR) due to high pressures in the bladder that overcome the normal antireflux mechanism is commonly seen in neurogenic bladders and can pose an additional challenge to management.

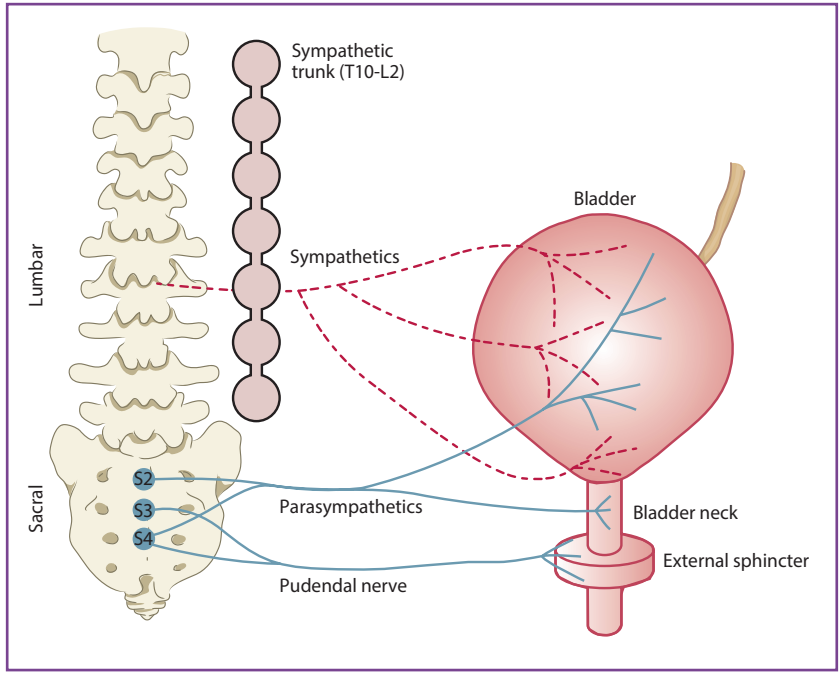

Figure 13-1. Schematic drawing of the bladder and urinary sphincter innervation.

Early closure of the NTD is usually performed by the neurosurgical team within 48 to 72 hours of birth. Most newborns with MMC will also have Arnold-Chiari malformation of the brain, with resulting hydrocephalus. Hydrocephalus is usually treated with a ventriculoperitoneal shunt, which is necessary to improve overall survival and reduce neurocognitive effects of the disease. Lower-extremity dysfunction is related to the degree of lumbar nerve involvement.

Diagnosis

Prenatal

In the age of advanced prenatal screening, most pregnant women in the United States undergo serum triple screening (or the "triple test") to determine levels of α-fetoprotein. Increased levels are suggestive of fetal NTD. Anatomic imaging scans between 17 and 20 weeks of gestation are now routine and can be used to diagnose most NTD prenatally.

A cystic sac with neural tube contents emanating from the spinal column is indicative of MMC. Other neural tube or vertebral anomalies, such as sacral agenesis, can also be detected prenatally. Many affected fetuses are now being detected and pregnancies terminated well before viability, which has, in part, reduced the incidence of this disease.

Newborn Assessment

Initial examination of a newborn with SB should be multidisciplinary, with urology, neurosurgery, orthopedics, and neonatal intensivist teams involved. In the case of MMC, urgent closure of the defect by a neurosurgeon is of paramount importance, as there is increased risk of meningitis.

There are no formal guidelines for urological assessment of the newborn with SB. In the past, a reactive approach was used, with urological workup occurring only if renal or bladder problems were detected. Today, most centers take a more proactive approach to determine baseline characteristics of the bladder and kidneys. Fifteen percent to 20% of newborns will have renal anomalies, and it appears that early intervention for "hostile" bladders will result in better long-term renal and bladder outcomes. Initial urological assessment typically includes renal and bladder ultrasonography (US) and serum creatinine level assessment (once a nadir is reached) to assess the renal anatomy and function. Bladder emptying may be impaired for life or only temporarily after back closure, so initial urethral catheterization is typically continuous after surgery. Once the back is sufficiently healed for the child to lay on the back or the side, the catheter is removed, and clean intermittent catheterization (CIC) of the bladder is typically initiated. The frequency of CIC is then adjusted on the basis of the residual urine volumes. Families are often taught CIC techniques, since this is the ultimate form of bladder management in up to 75% of adolescents and adults with MMC.

Urodynamic testing of bladder function is usually performed after discharge from the nursery. This study provides valuable information of bladder capacity, storage pressures (compliance), presence of uninhibited bladder contractions, and sphincter physiology. Urodynamic testing is often performed with fluoroscopic imaging of the bladder (videourodynamics); if not, voiding cystourethrography is ordered to evaluate the patient for VUR, as well as the appearance of the bladder, urethra, and sphincteric region.

Sacral Anomalies and Closed Neural Tube Defects

There are several types of occult spinal dysraphisms and sacral anomalies that can result in neurogenic bladder. In newborns with closed NTD, gluteal cleft asymmetry, sacral dimple, or hair tuft may clue clinicians in to the diagnosis of occult SB and are indications for spinal cord assessment (**Figure 13-2**). Spinal US is possible within the first 2 to 3 months after birth, since the posterior aspects of the spine have not yet ossified; thereafter, magnetic resonance imaging is required to visualize abnormalities of the cord. In addition to detection of neurocutaneous lesions, a tethered cord may be present if the conus is located below the midbody of L2. When these patients are assessed as newborns or during infancy, most have normal neurological examination findings, which can often be misleading. Urological workup in newborns with closed NTD or tethered cord should include renal and bladder US and urodynamic testing. Urodynamic testing may demonstrate abnormal lower urinary tract function in approximately one-third of infants with closed NTD.

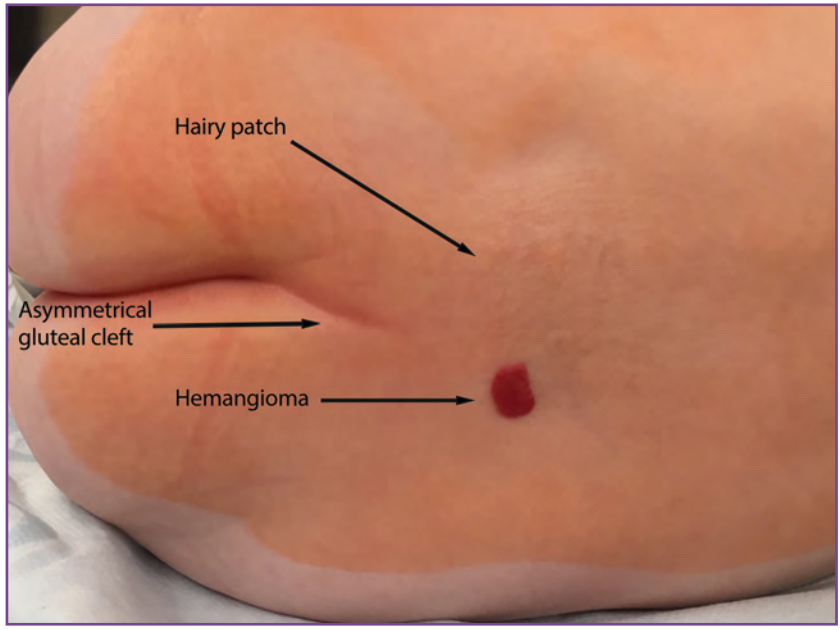

Figure 13-2. This infant's back demonstrates several findings associated with occult spinal dysraphism, including an asymmetrical gluteal cleft, a hairy patch over the sacrum, and a hemangioma.

Sacral agenesis is defined by the absence of part or all of 2 or more lower vertebral bodies and can result in neurogenic bladder. Prenatal diagnosis has increased with near-universal use and refinement of prenatal US. If not diagnosed prenatally or in early infancy, it may manifest with an inability to toilet train in school-aged children. Urodynamic evaluation and baseline renal and bladder US are recommended at the time of diagnosis.

Bladder management for closed NTDs and sacral agenesis is similar to that for cases of open NTDs. The primary difference is due to diagnosis at later ages on the basis of findings at physical examination or an inability to attain bladder control at a normal age (typically by the fourth birthday).

Treatment Options and Outcomes

The primary goals of urological management of neurogenic bladder throughout life are preservation of renal function and minimization of UTI development. Secondary goals evolve with age. By school age, attainment of urine and fecal continence is desired by most for proper socialization. For adolescents and young adults, independence and sexual function gain importance. Hopefully, by young adulthood, patients are ready to transition to adult providers and, thus, transitional care takes priority.

Treatment of neurogenic bladder continues to evolve as children age. With a lack of consensus on guidelines, practice patterns can vary by region or individual provider. Typically, patients with SB are followed up in multidisciplinary clinics with neurosurgery, orthopedics, urology, physical rehabilitation, and developmental pediatrics. However, since these multidisciplinary clinics are typically at tertiary centers, primary care pediatricians need to work collaboratively with these clinics to manage routine health care needs and simple urgent needs of these children.

Current treatment controversies include prenatal versus postnatal closure of MMC, early proactive versus expectant bladder management, interval of urological imaging and follow-up, and treatment of bacteriuria.

Prenatal Closure

After early prenatal detection, an increasing number of tertiary centers are now able to close MMC defects prenatally in select patients. A National Institutes of Health–sponsored, multicenter, randomized controlled trial to compare prenatal and postnatal closure (MOMS, the Management of Myelomeningocele Study) recently released its initial long-term results. Patients undergoing prenatal closure had a decreased need for ventriculoperitoneal shunt placement to manage hydrocephalus and had better lower-extremity neuromotor function and ambulation. Urological results, thus far, have been less promising, with no significant difference noted in urodynamic parameters, need for CIC, or need for later reconstructive surgery. Prenatal MMC closure was associated with increased risks of pregnancy complications, including preterm delivery, placental abruption, and uterine dehiscence. At this time, longer-term follow-up and investigation are needed to determine if the benefits truly outweigh the substantial risks and which patients will benefit the most.

Early Intervention Versus Expectant Bladder Management

Some advocate for early intervention in bladder management, with neonatal initiation of CIC and anticholinergic medication in all patients with SB to ensure regular and complete bladder emptying and to keep bladder storage pressures as low as possible. Proponents argue that early intervention provides better family and patient acceptance of CIC, better long-term renal outcomes, and a decreased need for later surgical reconstruction of the bladder. There is consensus that patients with "hostile" bladders at initial urodynamic testing need such management, but the controversy involves those with low-risk bladders and normal upper tracts.

Truly expectant management is guided only by changes in clinical symptoms. A more proactive expectant approach involves routine imaging and urodynamic testing to detect changes in bladder or renal function. It is well recognized that some neurogenic bladders will convert from low risk to high risk, since up to 50% of children with SB will demonstrate upper tract changes by age 5 (up from 15%–20% of newborns).

Proponents of expectant management argue that upper tract changes are reversible, and this approach prevents unnecessary morbidity of treatment and reduces familial stress with early intervention. CIC and anticholinergic medication are initiated if bladders become high risk or if upper tract changes are detected. If the bladder remains low risk, intervention is started only if needed to attain continence.

There is no consensus about follow-up intervals. The U.S. Centers for Disease Control and Prevention research protocol for urological management of the newborn and young child with SB was designed to provide evidence-based guidelines for follow-up and management. In this protocol, children are followed up with serial US every 3 months in the first year after birth, every 6 months in the second year, and annually thereafter. US provides a noninvasive method without radiation to detect hydronephrosis that may result from high bladder storage pressures and/or VUR. Urodynamic testing is repeated yearly until the third birthday. Other protocols recommend less frequent imaging and fewer or more urodynamic tests.

There has been no direct randomized comparison between early intervention and expectant management, but several prospective studies have been conducted to evaluate each approach. A few studies have demonstrated high-resolution rates (70%–90%) of upper tract changes with expectant management when CIC and anticholinergic medication were initiated after worsening upper tract changes. Comparison of an expectant versus a proactive approach showed that patients on the expectant protocol have higher rates of upper tract changes in the first 5 years after birth and higher rates of surgical intervention (vesicostomy and bladder augmentation) than those in the proactive group. However, the overall rates of renal deterioration once treatment was initiated were low in both groups, at less than 2%. Although prevention of renal deterioration is the ultimate goal in management, preventing morbidity of surgery is also important and may sway pediatric urologists and parents away from expectant management.

As the child grows and the spine elongates, there can be retethering of the cord. This may result in changes in bladder innervation and function, as well as changes in lower limb function. Repeat urodynamics testing will demonstrate these changes, if present, and guide therapy.

Complications of Neurogenic Bladder

Urinary Tract Infections

UTIs are the most common cause of morbidity and the number one acute diagnosis treated in emergency, inpatient, and outpatient settings in this population. Guidelines for diagnosis and treatment of UTI are variable; thus, these patients are at risk for overtreatment and antibiotic resistance, which can pose a medical and economic burden on the patient and family.

Many children with SB are managed with CIC and, thus, have an increased incidence of bacteriuria. It is a diagnostic dilemma to both community pediatricians and specialists to differentiate between urinary tract colonization (which should not be treated) and infection (which should). These patients may not have typical symptoms with UTI and may present with nonspecific symptoms, such as abdominal or lower back pain, dysuria, suprapubic pain, hematuria, foul-smelling urine, or increased incontinence. Recommended criteria for diagnosis of UTI include *(a)* positive urinalysis result, with more than 10 white blood cells per high-powered field; *(b)* positive urine culture result, with more than 100,000 colony-forming units per milliliter of a single organism; and *(c)* temperature higher than 100.4°F (38.0°C) or 2 other general symptoms (given earlier). UTI in this population can have increased morbidity due to delayed presentation and additional comorbidities; therefore, patients may need hospitalization and intravenous antibiotics.

Historically, antibiotic prophylaxis was widely used in patients treated with CIC to prevent UTI, but several contemporary studies show no benefit and demonstrate increased risk of antibiotic resistance. Antibiotic prophylaxis is, therefore, reserved for patients with moderate- to high-grade VUR or frequent culture-proven, symptomatic UTI.

Renal Deterioration

Long-term injury to the kidneys in patients with neurogenic bladder is a real and serious threat, and all providers must be diligent in its prevention. In patients who receive proper management, the risk of renal injury is low but not insignificant, and end-stage renal disease does occur at younger ages than in the general population. Hostile bladders with high storage pressure, decreased capacity, and decreased

compliance can be deleterious to the kidneys. Even in the absence of VUR, the high bladder pressures can be transmitted to the kidneys because the bladder pressure exceeds the ureteral emptying pressure, and imaging will show the resultant hydronephrosis and, potentially, renal cortical thinning. Secondary VUR and increased risk of UTI can further accelerate renal injury.

Urinary Incontinence

Although not life-threatening, urinary incontinence can have a negative effect on patient quality of life. Incontinence can be caused by bladder dysfunction (ie, decreased capacity, increased storage pressure [poor compliance], or detrusor overactivity [uninhibited contractions]) and/or sphincter incompetence. Most patients can achieve continence with pharmacotherapy and/or CIC, but some cannot achieve it without surgical intervention to improve bladder capacity and compliance and/or increase bladder outlet resistance. Interestingly, recent studies have shown that quality of life is more negatively affected by the quantity than the frequency of urinary incontinence. Incontinence can have medical consequences in the form of genital, perineal, and gluteal skin ulceration and breakdown. Incontinence is often managed with pads, liners, or diapers, depending on the volume of leakage and patient preference.

Urodynamic Testing

As mentioned previously, urodynamic testing has become an integral tool in managing neurogenic bladders in children. The study can provide valuable information on bladder capacity, bladder pressures, and sphincteric function to identify children with hostile bladders that put them at risk for upper tract injury. Any suspicion of neurogenic bladder or associated etiologic origins is an indication for baseline urodynamic testing and likely repeat testing throughout childhood. Conducting an initial study within the first 3 months after birth in infants with congenital neurogenic bladder is useful in providing baseline information on bladder and sphincter function and may aid in management. In those with acquired neurogenic bladder, testing may be appropriate at the time of diagnosis or before neurosurgical management. In cases of spinal cord injury or after surgery, testing is typically delayed for 6 months to allow an initial period of neurological stabilization.

Urodynamic testing should be performed by trained nurses and physicians and with the child awake, if possible. Verbal and nonverbal feedback is important to be able to gauge the patient's sensation of bladder filling, as well as to allow those who are capable of voiding to do so. Studies performed with general anesthesia are less physiological and less accurate.

Urodynamic testing comprises several components: cystometrography, electromyography (EMG) of the sphincter, uroflowmetry, and, often, fluoroscopy. Pressure-sensing catheters are placed in the bladder (via the urethra) and the rectum, and the bladder catheter has a second lumen to allow simultaneous bladder filling. EMG skin patches or, less commonly, needles are placed on or in the perineum to detect sphincteric activity. There are typically 2 phases to the cystometrogram: filling and voiding cystometry. Multiple filling cycles are sometimes needed, particularly in infants. **Figure 13-3** illustrates a typical urodynamic testing setup, including a fluoroscopy C-arm unit for videourodynamics.

The bladder is filled over 10 to 20 minutes with saline (or radiopaque contrast material if fluoroscopy is used [videourodynamics]), while bladder (detrusor) pressure is closely monitored. A normal bladder has an expected capacity equal to [(patient age + 2) × 30] milliliters, and the detrusor pressure should not increase above 15 cm of water, indicating normal compliance (**Figures 13-4** and **13-5**).

The presence of detrusor overactivity, defined by uninhibited bladder contractions over 15 cm of water, is a sign of neurogenic bladder. A steady rise in detrusor pressure in the absence of a contraction represents decreased compliance (**Figures 13-6** and **13-7**). In the setting of high bladder pressures, characterization of sphincteric function becomes important. The pressure at which leakage occurs in the absence of a contraction is termed the *detrusor leak point pressure,* and a value higher than 40 cm H_2O has been strongly linked to renal deterioration. With sphincter incompetence, leakage occurs at lower pressures, which protects the kidneys but leads to persistent incontinence.

During the voiding phase, voiding pressure and sphincteric activity should be observed. There should be coordination between the detrusor and sphincter to allow relaxation of the sphincter (decreased EMG activity) during voiding when the detrusor contracts to expel the urine

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Figure 13-3. Typical setup of urodynamic testing with a fluoroscopy unit for video urodynamics.

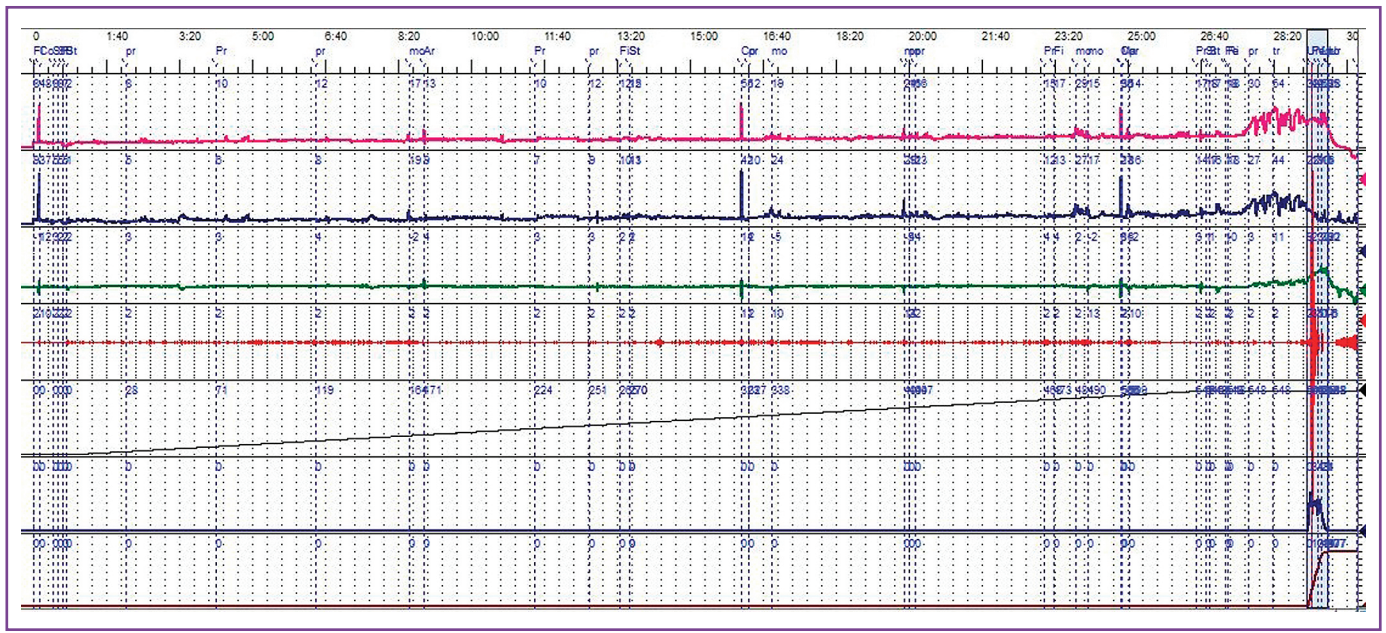


Figure 13-4. Videourodynamics of a normal bladder. The bladder pressure (top line, in magenta) and abdominal pressure (second line, in navy) are measured as the bladder is filled (infused volume is noted on the fifth line, in black). The detrusor pressure (third line, in green) remains flat until the patient noted bladder fullness and was given permission to void. The detrusor pressure then increases modestly as the bladder contracts to empty. The electromyography tracing (fourth line, in red) shows an initial increase as the patient contracts the sphincter to prevent voiding but then relaxes typically to allow bladder emptying. The urinary flow pattern is a normal bell-shaped curve on the sixth line, and the voided volume is recorded on the bottom line.

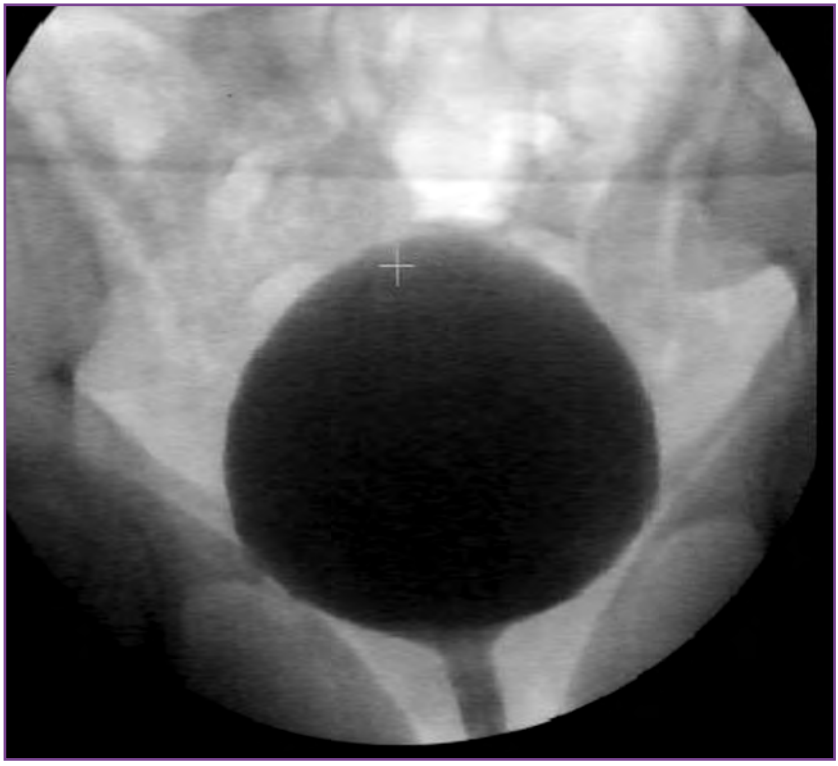


Figure 13-5. Fluoroscopic image of a normal bladder, obtained during voiding, shows a spherical, smooth-walled bladder with an open bladder neck and cylindrical female urethra.

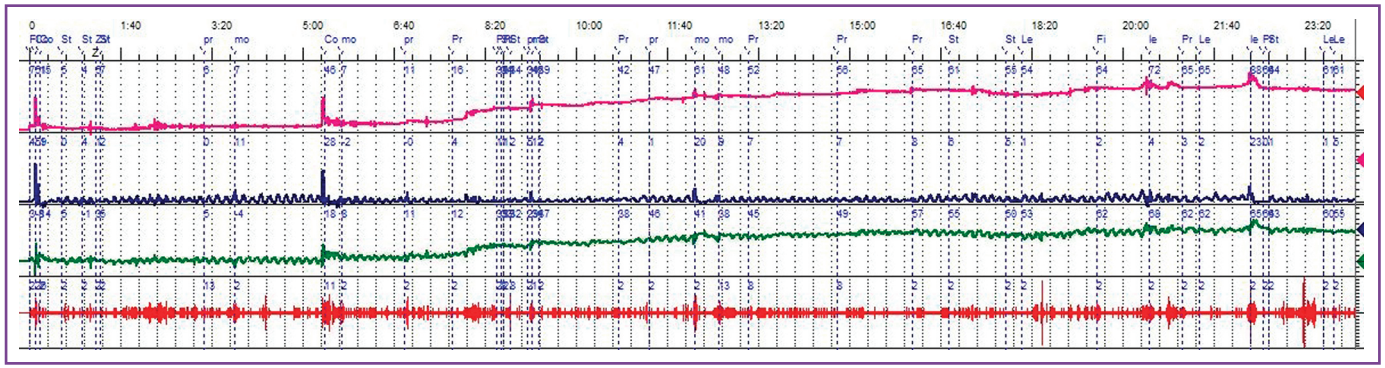


Figure 13-6. Videourodynamics of a bladder with poor compliance (hostile bladder). The bladder pressure (top line, in magenta) shows a steady increase during bladder filling, while the abdominal pressure (second line, in navy) remains essentially flat during bladder filling. The detrusor pressure (third line, in green) mimics the bladder pressure curve. The electromyography tracing (fourth line, in red) shows increased sphincter activity with filling and associated bursts of activity, with the instantaneous increases in bladder pressure seen as spikes on the bladder (magenta) and detrusor (green) curves. This patient did not void, so not all rows are shown.

Figure 13-7. Fluoroscopic image of an "end-stage" neurogenic bladder with poor compliance, demonstrating an oblong shape and severely trabeculated wall (irregular edges). The urethra is dilated down to a closed sphincter in this patient with detrusor-sphincter dyssynergia. This patient received medical therapy but failed to achieve continence with anticholinergics and intravesical onabotulinumtoxinA and ultimately required bladder augmentation.

(see **Figure 13-5**). Detrusor-sphincter dyssynergia is commonly seen in children with lumbar or higher spinal cord injuries or MMC and is defined by increased EMG activity during voiding (or during an uninhibited contraction) (see **Figures 13-6** and **13-7**). More often than not, children with neurogenic bladder have difficulty voiding and, thus, the voiding phase may not be possible.

Videourodynamic testing is simply the addition of cystography via fluoroscopy. Imaging can provide useful information on bladder contour

(smooth-walled versus trabeculated [indicative of severe neurogenic bladder]), bladder neck anatomy (open or closed) during voiding and leakage, and presence of VUR (**Figure 13-8**).

Hostile bladders are defined by reduced bladder capacity, poor compliance, detrusor leak point pressure higher than 40 cm H_2O, dyssynergia, trabeculation, and high-grade VUR. Children and their bladders are dynamic, so urodynamics parameters can change, sometimes with surprising rapidity. Regular testing is recommended to detect changes in neurogenic bladder (see the previous discussion).

Figure 13-8. Vesicoureteral reflux noted at videourodynamic imaging. This patient presented with recurrent urinary tract infections and a scarred, poorly functioning left kidney and was lost to follow-up. The fluoroscopic image shows a small trabeculated bladder that maintained relatively low pressure by refluxing a larger volume of urine into the massively dilated left ureter and kidney (kidney not shown). The patient underwent left nephroureterectomy and bladder augmentation.

Pharmacotherapy

Anticholinergic Medications

Anticholinergic medications are first-line agents for neurogenic bladder, to reduce detrusor overactivity and/or improve compliance by lowering storage pressures. The bladder wall smooth muscle contains muscarinic receptors M_2 and M_3. M_2 receptors are in abundance, but M_3 receptors primarily mediate muscle contractions. Anticholinergic medications competitively inhibit binding of acetylcholine to the muscarinic receptors to prevent smooth-muscle contraction. Response rates for most anticholinergic medications are generally good. By improving overactivity and compliance, anticholinergic medications have been shown to increase bladder capacity, reduce deleterious pressure, and decrease incontinence episodes.

Since muscarinic receptors are found throughout the body, most nonspecific antimuscarinic medications have varying degrees of adverse effects, such as dry mouth, dizziness, headache, blurred vision, facial flushing, and constipation. There have been some concerns for long-term cognitive effects, but small prospective, randomized trials have shown no short-term negative effects of these medications on attention or memory in children. In general, it is believed that these medications are safe for children, as long as the side effects can be tolerated.

Oxybutynin is the only FDA-approved antimuscarinic medication for children with neurogenic bladder. It is available in both immediate-release (liquid and pill) and once-daily long-acting (pill only) oral formulations, as well as transdermal formulations. Oral administration is usually 0.2 mg/kg per dose up to 3 times daily. The transdermal dose is 3.9 mg daily for adults and may be used in lieu of oral forms to reduce systemic side effects. Intravesical use of oxybutynin has been well studied with adequate outcomes and can be used if the medication is not tolerated by mouth. Oxybutynin tablets can be dissolved in tap water and then instilled after the bladder is emptied by means of catheterization.

Three other anticholinergic medications—tolterodine, fesoterodine, and solifenacin—are not FDA approved in children but have been shown to be effective and well tolerated in children. Side effects are similar to those of oxybutynin but may differ in individual patients.

Adrenergic Agonist Medication

Mirabegron is a relatively new agent with similar inhibitory effect on the bladder through a different mechanism. It is a β_3-adrenergic agonist and does not have the antimuscarinic side effects associated with older bladder medications. The medication has not been approved by the FDA for use in children, but early studies show it to be effective and safe. The main adverse effect is hypertension.

OnabotulinumtoxinA

Another alternative to anticholinergic medication is intradetrusor injection of onabotulinumtoxinA, a neurotoxin produced by the gram-positive bacterium *Clostridium botulinum* that inhibits acetylcholine release, resulting in muscle paralysis. It is FDA approved for treatment of neurogenic urinary incontinence and detrusor overactivity in adults, but multiple studies have shown it to be effective and safe in children. Accordingly, it is a second-line agent for patients who do not achieve continence with the previously named medications or cannot tolerate the side effects. It is usually administered in the operating room, with anesthesia. The medication is injected directly into the bladder muscle under direct vision, via a cystoscope. Clinically, patients have improved dryness between catheterizations. The duration of response ranges from 6 to 12 months; thus, parents and children should know that they will require repeat procedures. Side effects are infrequent but include UTI, hematuria, and urinary retention (problematic if not performing CIC).

Neuromodulation

Neuromodulation is another treatment modality available for some children with neurogenic bladder. The Interstim (Medtronic, Minneapolis, MN) sacral neuromodulation device involves permanent electrical stimulation of the sacral nerves at the S3 level by using an implantable pulse generator device to modulate bladder function. It is FDA approved for treatment of urinary retention and symptoms of overactive bladder, including urge incontinence and urgency and frequency in patients aged 16 years and older who have not achieved continence with more conservative therapies. Sacral neuromodulation was initially studied in younger children with nonneurogenic bladder and had promising outcomes. A small prospective study showed increase in bladder capacity and decrease in detrusor leak point pressure

in the neuromodulation group, but other urodynamic parameters were unchanged. The implantable device and wires can be a nidus for infection or become dislodged in active children, necessitating revision or repositioning. The results thus far are limited, but larger-scale studies are being conducted. Its use in individuals with prior spinal cord surgery, including nearly all children with SB, remains experimental, since lead placement can be challenging.

Surgical Intervention

The primary indications for surgery for neurogenic bladder are *(a)* presence of renal deterioration despite maximal medical management or *(b)* desire for urinary continence and social independence in older children to improve quality of life (if CIC and anticholinergic medication have been unsuccessful or not possible). Prior to the 1970s, incontinent urinary diversion to an external appliance was the mainstay of urological management of SB to bypass the hostile bladder. With the advent of urodynamic testing, CIC, and pharmacotherapy, continent surgical reconstruction by using the bladder has gained popularity and is now the standard of care when indicated. These procedures include bladder augmentation with or without bladder neck reconstruction and/or continent catheterizable channel.

Incontinent diversion with cutaneous vesicostomy is used currently in mostly young children in whom continence is not an issue and who may be too young for reconstructive surgery. Indications typically include hostile bladder and/or recurrent pyelonephritis that is unresponsive to conservative therapy or patient/family noncompliance with therapy. In older patients or those with advanced renal disease, diversion to an external appliance by using a bowel conduit is sometimes still performed.

Bladder augmentation is first-line surgical management for bladders with low capacity and/or high pressures, despite maximal medical management (**Figure 13-9**).

Typically, enterocystoplasty involves the use of a segment of ileum or sigmoid colon as a patch to enlarge the bladder. A large, low-pressure reservoir for urine storage is thus created, and emptying can only occur via CIC. For those who cannot or will not catheterize via the urethra, a continent catheterizable channel from the bladder to the abdominal

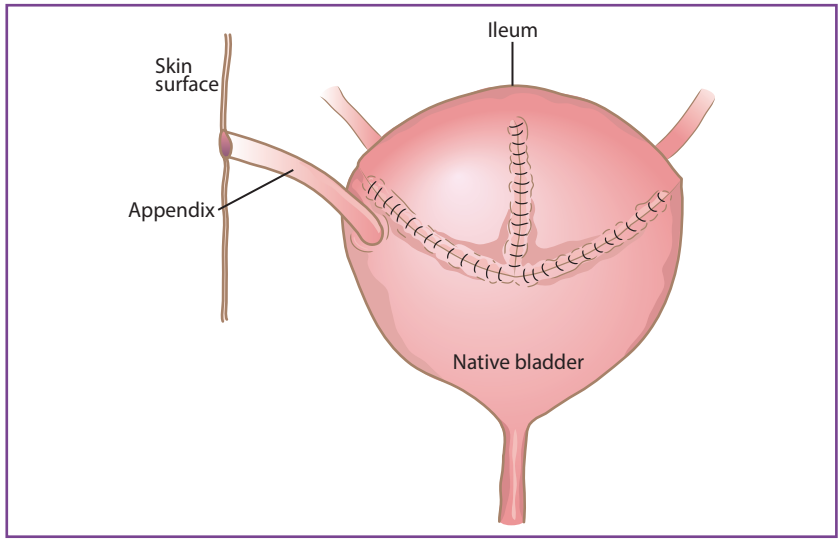


Figure 13-9. Illustration depicting an augmentation enterocystoplasty by using a portion of ileum. With bladder augmentation, the aim is to increase bladder capacity while reducing detrusor pressures. The appendix or a smaller segment of ileum can be used to create a continent catheterizable channel between the bladder and the umbilicus.

wall or umbilicus can be created by using the appendix (Mitrofanoff) or reconfigured ileum (Monti).

Enterocystoplasty is highly effective but not without significant short- and long-term complications, including infection, stone formation, bowel obstruction, electrolyte imbalances, osteopenia, bladder perforation, and bladder tumors. Vitamin B_{12} deficiency can also occur a number of years after augmentation, and blood levels should be checked periodically in all these children. Bladder perforation is a potentially fatal complication that requires emergent surgical exploration; it results from bladder overdistention from lack of emptying due to patient neglect or inability to catheterize. Catheterizable channels likewise have relatively frequent complications, including stomal stenosis and channel injury with catheterization that also may necessitate urgent surgery.

The procedures herein will not achieve continence for patients with sphincteric incompetence, and bladder neck procedures may be indicated to increase bladder outlet resistance. There are numerous procedures that range from occlusive slings to bladder neck reconstructions to

bladder neck closures. A bladder neck sling created by using autologous fascia, biological graft, or synthetic material is used most commonly. Bladder neck reconstruction is more involved but may have greater durability. A continent catheterizable channel is usually created concomitantly because the bladder neck occlusion makes CIC via the urethra difficult. Bladder neck closure is less popular in children because of high complication rates and the fact that there is no longer a "safety valve" for urine to exit through if the child is not compliant with CIC. The most common complication of the bladder neck procedure is persistent urine leakage that can be addressed with injection of a bulking agent or surgical revision.

Neurogenic Bowel

Most patients with neurogenic bladder will have concomitant neurogenic bowel, manifesting with severe constipation and/or fecal incontinence. Fecal incontinence more negatively affects quality of life than does urinary incontinence. Management includes dietary modification, laxatives, enemas, and digital stimulation and/or disimpaction and must be tailored to the patient's anal sphincter tone, mobility, manual dexterity, and caregiver support. Standard enemas may fail in those with lax sphincter tone, and the use of a cone enema device or balloon catheter may be indicated. Refractory constipation or incontinence may be addressed surgically to allow antegrade enemas to evacuate the colon. In a Malone antegrade continence enema ("MACE") procedure, the appendix or cecal flap is brought to the skin as a small, continent stoma (**Figure 13-10**).

This is frequently done at the same time as bladder reconstruction surgery. The stoma is then catheterized every 1 to 3 days, and fluid is instilled in the colon to push stool downstream and out the anus. Alternatively, a cecostomy or Chait tube can be placed to allow similar access to the cecum, but the device is visible and must be changed with regularity. Common complications of antegrade continence enema include leakage from stoma and stomal stenosis. In general, the use of antegrade continence enema has been shown to significantly improve fecal continence, decrease the time dedicated to the bowel regimen, and improve the quality of life for both child and caregiver.

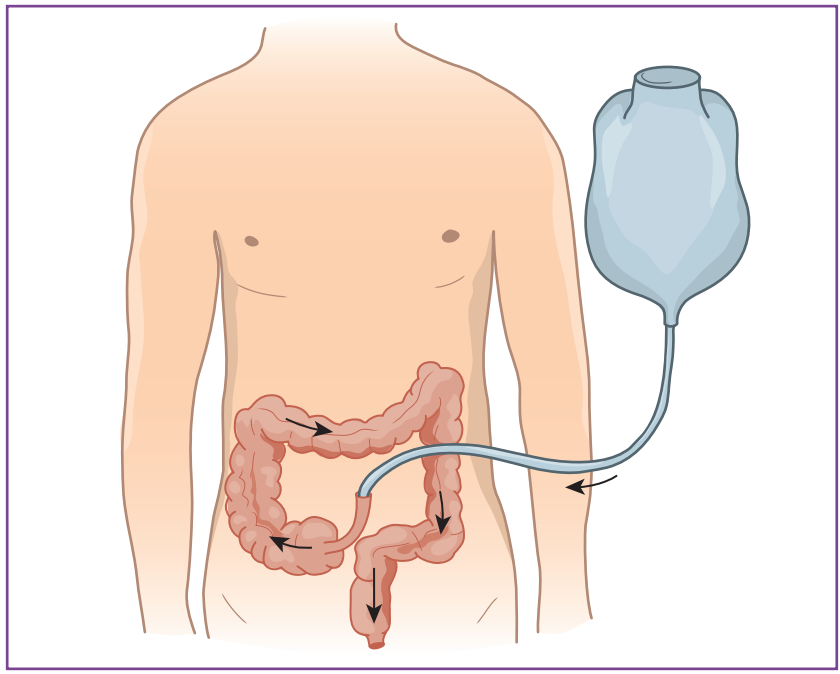


Figure 13-10. Illustration depicting a Malone antegrade continence enema channel during bowel irrigation. The appendix is brought up to the umbilicus as a continent stoma. The colon is flushed with irrigation every 1 to 3 days to flush stool downstream and out of the anus.

When to Refer

- Children with neurogenic bladder should undergo routine follow-up with a urologist, neurosurgeon, physical rehabilitation medicine specialist, or other specialists.
- Children with SB are usually examined in a multidisciplinary clinic at least 1 to 2 times per year, but the day-to-day issues will often be handled by primary care physicians.
- Refer the patient to or initiate direct communication with a pediatric urologist for the following indications:
  - — Recurrent culture-proven UTIs, especially if associated with fevers and known VUR.
  - — New-onset or worsening urinary or fecal incontinence.
  - — Serial imaging follow-up or any changes to upper tracts, such as new or worsening hydronephrosis.

— If a patient has had prior reconstructive surgery, any issues with catheterizing through the stoma, inability to empty the bladder, or urinary leakage; if the patient has not been catheterized in more than 6 hours, his or her pediatric urologist must be notified immediately.
— If a patient has a bladder augmentation and diffuse abdominal pain with fever or signs of sepsis; this is considered a bladder perforation until proven otherwise, and patients should be sent to a hospital capable of performing a cystogram in a child.

Clinical Pearls

- Neurogenic bladder can be caused by various congenital or acquired disease processes, but the management tends to be the same.
- Management will consist of serial imaging of the kidneys and bladder, urodynamic studies conducted at various points in the child's life, with or without intermittent catheterization and with or without pharmacotherapy, to optimize bladder function and prevent upper tract damage.
- Surgical reconstruction with bladder augmentation, bladder neck reconstruction, and catheterizable channel are options if medical management fails, but surgery can be morbid with high complication rates.
- Recommended criteria for diagnosis of UTI include *(a)* positive urinalysis result with more than 10 white blood cells per high-powered field; *(b)* positive urine culture result with more than 100,000 colony-forming units per milliliter of a single organism; and *(c)* temperature higher than 100.4°F (38.0°C) or 2 other general symptoms.
- Concomitant treatment of neurogenic bowel is important, to decrease rates of fecal incontinence and UTI.

Resources for Parents

- Spina Bifida Association. http://spinabifidaassociation.org. Accessed October 17, 2018
- Urology Care Foundation. What is neurogenic bladder? http://www.urologyhealth.org/urologic-conditions/neurogenic-bladder. Accessed October 17, 2018

Suggested Readings

MacLellan DL, Bauer SB. Neuromuscular dysfunction of the lower urinary tract in children. In: Wien AJ, ed. *Campbell-Walsh Urology.* 11th ed. Philadelphia, PA: Elsevier; 2016:3272–3296

Bauer SB, Austin PF, Rawashdeh YF, et al; International Children's Continence Society. International Children's Continence Society's recommendations for initial diagnostic evaluation and follow-up in congenital neuropathic bladder and bowel dysfunction in children. *Neurourol Urodyn*. 2012;31(5):610–614

Lapides J, Diokno AC, Silber SJ, Lowe BS. Clean, intermittent self-catheterization in the treatment of urinary tract disease. *J Urol*. 1972;107(3):458–461

Clayton DB, Brock JW III, Joseph DB. Urologic management of spina bifida. *Dev Disabil Res Rev*. 2010;16(1):88–95

Ross SS, Wiener JS. Practical urodynamics in children. In: Peterson AC, ed. *Practical Urodynamics for the Clinician*. Cham, Switzerland: Springer; 2016:143–159

Routh JC, Cheng EY, Austin JC, et al. Design and methodological considerations of the centers for disease control and prevention urologic and renal protocol for the newborn and young child with spina bifida. *J Urol*. 2016;196(6):1728–1734

Madden-Fuentes RJ, McNamara ER, Lloyd JC, et al. Variation in definitions of urinary tract infections in spina bifida patients: a systematic review. *Pediatrics*. 2013;132(1):132–139

Snow-Lisy DC, Yerkes EB, Cheng EY. Update on urological management of spina bifida from prenatal diagnosis to adulthood. *J Urol*. 2015;194(2):288–296

Clayton DB, Tanaka ST, Trusler L, et al. Long-term urological impact of fetal myelomeningocele closure. *J Urol*. 2011;186(4 Suppl):1581–1585

CHAPTER 14

The Pediatrician's Role in Assessing Disorders of Sex Development in Newborns

Erin R. McNamara, MD, MPH; Jonathan M. Swartz, MD, MMSc; and David A. Diamond, MD, FAAP

Introduction

Disorders of sex development (DSD) is the terminology proposed by the 2006 "Consensus Statement on Management of Intersex Disorders" to replace the historical term *intersex.* It broadly encompasses congenital conditions in which development of chromosomal, gonadal, or anatomic sex is atypical. This change in nomenclature reflected the change in attitude toward these disorders as the understanding of genetics improved and as practitioners recognized the pejorative nature of certain terms. There remains controversy over terminology, and sensitivity is imperative when discussing evaluation and diagnosis with families.

History

Historically, sex assignment in the setting of ambiguity was deferred to the obstetrician and/or pediatrician. Early evaluation and diagnosis were encouraged to limit the stress to parents and to start rearing the child early in the selected gender role. It was commonly believed that surgical intervention should be completed within the first 2 years after birth to avoid psychological distress and take advantage of the early plasticity in developing gender identity. In addition, families were encouraged to limit discussion with "outsiders" and to "tell as few people as possible." There have been marked changes in care of the newborn with DSD. In 2006, with the publication of the consensus statement, many of these issues were highlighted and helped form the current management strategies of patients with DSD.

Epidemiology

The incidence of the full range of DSD is 1 in 1,500 births, with more severe ambiguity seen in 1 in 5,000 births. In the newborn period, DSD is most often diagnosed because of ambiguous genitalia. Given the complexity and heterogeneity of these disorders, it is helpful for the pediatrician to know which patients warrant evaluation and who should be involved in the care of these patients. In addition, the pediatrician will provide continuity of care throughout all stages of childhood.

Development

To be able to understand the spectrum of DSD, it is crucial to understand normal sex development. The Jost paradigm has been used for years to describe the 3 components in sex development. The first is chromosomal sex, which is determined at the time of conception. The second is gonadal determination, which occurs by the sixth week of gestation. The bipotential gonad is affected by the presence or absence of certain genes, of which the *SRY* gene (the sex-determining region of the Y chromosome) is the most important in humans, providing the biological switch for the gonad to become a testis. The third component is anatomic sex differentiation, whereby the gonad and elaboration of hormones determines the phenotypic sex.

In the presence of *SRY,* the gonad forms Leydig cells that produce testosterone and insulin-like factor 3 (INSL3). Locally, on the side of the gonad, through passive diffusion, testosterone plays a role in the development of the wolffian structures of the male. Peripherally, testosterone is converted by 5α-reductase to dihydrotestosterone, which is responsible for the development of external male genitalia, including the phallus, urethra, and scrotum. INSL3 is thought to contribute to testicular descent. In addition, testicular Sertoli cells produce antimüllerian hormone (AMH) and inhibin B. AMH is responsible for the regression of the müllerian structures during male sex differentiation, concordant with the 46,XY chromosomal sex. Both androgens and AMH produced by the testes are paracrine in nature and act locally on the side of the gonad.

For several decades, it was taught that the female phenotype was the default pathway. However, more recently, it has been shown that there are several factors involved in female sex differentiation and that the process of normal sex development is much more complex than the Jost paradigm. In the absence of *SRY* and in the presence of other genes such as *WNT4*, *RSPO1*, and *FOXL2*, the bipotential gonad will become an ovary. The ovary does not produce AMH; therefore, müllerian structures are maintained, while the lack of testosterone prevents wolffian structures from persisting.

Development includes a complex coordination of chromosomal factors, gonadal function, internal genitalia, external genitalia, and even gender identity and gender role. There is ongoing research into the contribution of these factors to sex development. See **Figure 14-1**.

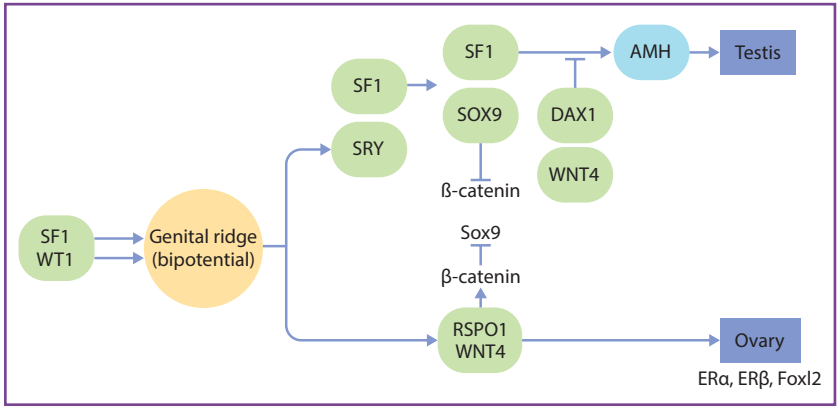


Figure 14-1. Differentiation of bipotential gonads.

Types of Disorders of Sex Development

This review will go over the most common types of DSD associated with ambiguous genitalia in the newborn—in particular, congenital adrenal hyperplasia (CAH). It is imperative to establish the diagnosis of CAH in the newborn period, and a well-informed pediatrician will be able to facilitate evaluation in the presence of ambiguous genitalia. We will also briefly discuss mosaicism, which may appear in the newborn period but can also manifest in adolescence. This nomenclature is recognized by the 2006 consensus statement, on the basis of karyotype results, and further categorized according to laboratory and imaging data.

46,XX DSD

46,XX DSD is the most prevalent form of DSD when nonclassical forms are included, and more than 90% of cases are attributed to CAH. CAH is an autosomal-recessive disorder that results from a deficient enzyme in the steroid biosynthetic pathway, which preferentially increases the production of androgens and leads to a virilized female (**Figure 14-2**).

21-hydroxylase (21-OH) deficiency is the most common cause of CAH (95%), and its salt-wasting form (seen in 75% of cases) can be life-threatening if not diagnosed early. Less common causes of CAH are 11 β-hydroxylase and 3 β-hydroxysteroid dehydrogenase deficiency. The endocrinologist will manage these cases with a careful titration of glucocorticoids and, in some cases, mineralocorticoids with salt supplementation. Physical examination findings demonstrate virilized external genitalia with nonpalpable gonads and internal genitalia consisting of vagina and uterus (**Figure 14-3A**). Laboratory data show increased serum 17-hydroxyprogesterone (17-OHP) levels in the 21-OH form of CAH.

46,XY DSD

46,XY DSD is a heterogeneous group, typically with variable degrees of undervirilization. A specific molecular diagnosis is established in fewer than one-half of cases. Undervirilization may occur for one of the following reasons: Leydig cell failure, testosterone biosynthesis enzyme deficiency and the less common forms of CAH (3 β-hydroxysteroid dehydrogenase deficiency, steroidogenic acute regulatory protein

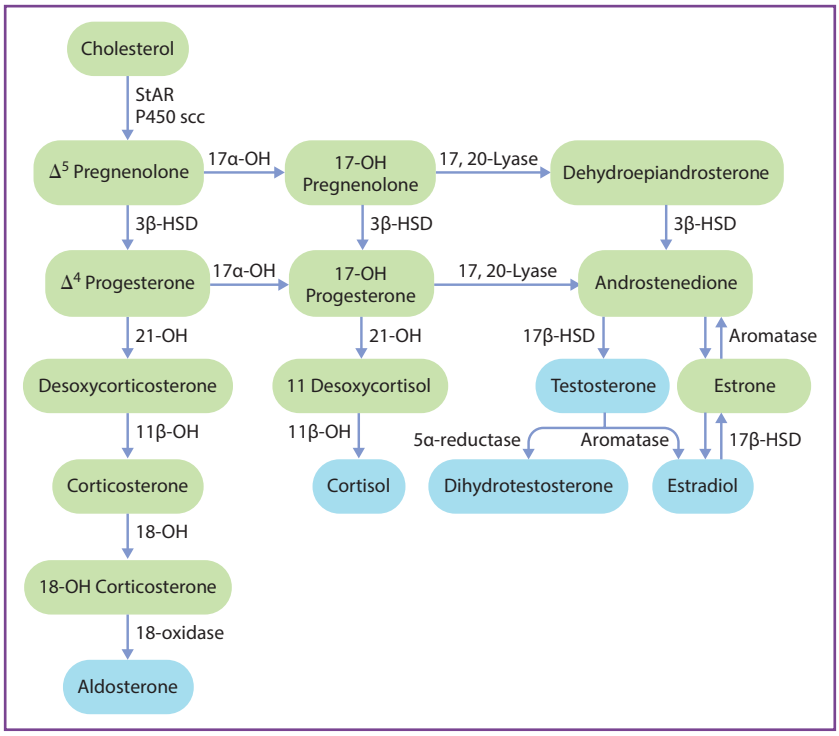


Figure 14-2. Steroid biosynthetic pathway. HSD, hydroxysteroid dehydrogenase; OH, hydroxylase; StAR, steroidogenic acute regulatory protein.

deficiency, and 17 hydroxylase deficiency), androgen insensitivity syndrome (complete or partial), 5α-reductase deficiency, and persistent müllerian duct syndrome. Most cases of 46,XY DSD that do not have a definitive molecular diagnosis are often categorized as partial androgen insensitivity syndrome (PAIS). Those with PAIS usually have severe hypospadias and may have micropenis (also called *microphallus*) (**Figure 14-3B**). In approximately 50% of patients with PAIS, a mutation on the androgen receptor can be identified. Complete androgen insensitivity syndrome (CAIS) is defined as having external female genitalia with testes that are intra-abdominal or palpable in the labia and a blind-ending vagina. Historically, these newborns often did not receive diagnoses until amenorrhea in puberty and were raised as female. Now with prenatal cell-free fetal DNA testing, prenatal diagnosis is becoming more frequent.

Figure 14-3. **A,** 46,XX congenital adrenal hyperplasia. **B,** 46,XY partial androgen insensitivity syndrome (micropenis and bilateral palpable undescended testicles). **C,** Mixed gonadal dysgenesis asymmetrical anatomy.

Sex Chromosomal DSD

Sex chromosomal DSD is the final category of DSD and is defined as the absence or addition of chromosomes or mosaicism. These may be diagnosed in the newborn period but often manifest during puberty because of amenorrhea or delayed puberty. Examples are Turner syndrome (45,X) seen in female patients and Klinefelter syndrome (46,XXY) seen in male patients. The most common form of mosaicism

is mixed gonadal dysgenesis (MGD) (45,X, 46,XY), typically with a unilateral streak gonad and contralateral dysplastic testis, which represents the second leading cause of ambiguous genitalia in the newborn (**Figure 14-3C**).

Prenatal Diagnosis

The ability to diagnose DSD prenatally is a rapidly changing area of medicine and is becoming more common. Historically, most DSD cases have been diagnosed in the newborn period. There are rare occasions in which the prenatal ultrasonographic (US) findings may demonstrate ambiguous genitalia; however, the screening US results at 13 to 15 weeks of gestation are neither specific nor sensitive for identifying ambiguous genitalia. Many prenatally diagnosed cases have a fetal karyotype that is incongruous with the US findings. Fetal karyotype, fluorescent in situ hybridization (FISH) for *SRY,* and amniotic hormone studies are all potential prenatal diagnostic studies for ambiguous genitalia; however, these require amniocentesis or chorionic villous sampling.

With the advent of noninvasive prenatal testing (NIPT) by using cell-free DNA, chromosomal sex can be determined as early as 7 weeks of gestation. The fetal DNA is derived from the breakdown of placental cells (which usually carry the same genetics as the fetus) that enter the maternal blood stream. This test has been extended to sex chromosome aneuploidy, but there are no robust estimates for sensitivity and specificity of sex chromosome abnormalities and mosaicism. This test may also be useful in early detection of CAH and can be offered to families with a history of early infant demise or known CAH but remains experimental for this purpose.

Prenatal diagnosis has increased over time. Overall, 25% of the DSD population seen in one multidisciplinary clinic received prenatal diagnoses, but of note, only 9% received diagnoses between 1994 and 1999, while 40% received prenatal diagnoses after 2006. This speaks to the improvement in imaging, as well as the availability of FISH technology and NIPT.

Postnatal Evaluation

As a pediatrician, involvement in the diagnosis and evaluation of DSD will be immediate. Over the years, it has been emphasized that a multidisciplinary team approach to these patients is essential. At a minimum, the pediatrician and/or neonatologist, endocrinologist, urologist, and psychologist should be involved in the initial discussion with the family. In addition, a geneticist and medical ethicist may be valuable members of the team. At each institution, this team may be organized a little differently, but most importantly, there should be agreement about approach to the diagnosis and communication with the family. Families will be alert to inconsistent advice from different stakeholders. There should be a team meeting to agree on a management approach, with one person designated as the spokesperson to decrease misunderstanding. The family should be deeply involved in the management decisions.

The pediatrician will usually decide who needs to be evaluated. The most common consultation will be for ambiguous genitalia; however, this includes a range of presentations. The following is a list of neonates that should be evaluated for DSD:

- Those with micropenis with bilateral nonpalpable gonads. The definition of *micropenis* is widely agreed to be a stretched penile length less than 2.5 cm in a full-term neonate. The mean penile length in a full-term neonate is 3.5 cm, and micropenis is less than 2.5 SDs below the mean. This does not include preterm newborns (see **Figure 14-3B**).
- Those with clitoromegaly, with or without a urogenital sinus. The definition of *clitoromegaly* is a length of more than 9 mm or a width of more than 6 mm in a full-term neonate (see **Figure 14-3A**).
- Apparent female external genitalia with a labial or inguinal mass.
- Hypospadias with unilateral nonpalpable testes and severe hypospadias with undescended testes.
- Prenatal chromosome evaluation that is discordant with the external genitalia.

Use of these guidelines may allow selectivity in the workup that is sometimes done for isolated micropenis or clitoromegaly. In the preterm neonate, it is important to know that the mean phallic length around 30 weeks' gestation is 2.5 cm ± 0.4, and isolated clitoromegaly can also be seen.

Goals of Evaluation

Once the initial evaluation has been completed and there is concern for ambiguous genitalia, there are 3 goals of the team evaluating the patient: identify life-threatening disorders, establish a diagnosis in a timely fashion, and counsel the family with regard to sex assignment. The evaluation of the newborn should always begin with a detailed history and physical examination. Laboratory data will be important to determine the genetic sex and rule out life-threatening causes of ambiguous genitalia. Imaging can be useful for identifying internal structures, as well as planning for future surgical intervention. Newer molecular techniques may provide more detailed information about the etiologic origins of DSD.

Diagnosis

History

A history is important in identifying potential causes of DSD. Maternal exposure to androgens could affect development. Previous neonate deaths may suggest salt-wasting CAH. Family history of female infertility or amenorrhea suggests androgen insensitivity. To avoid overwhelming the family, one member of the multidisciplinary team should obtain a thorough family history. While this information can be useful, the subsequent physical examination findings and laboratory and/or imaging results are rarely changed on the basis of the family history.

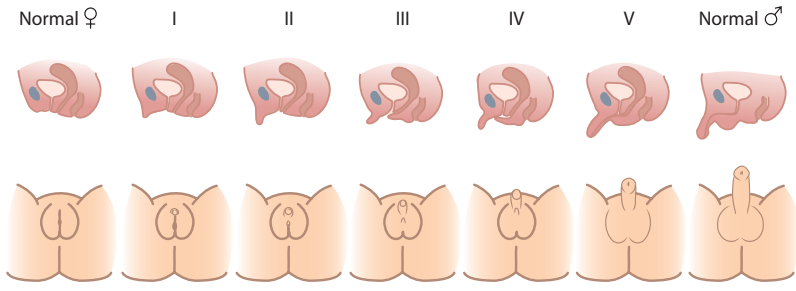
Physical Examination

The physical examination can be difficult in the newborn, and a combined examination with the pediatric urologist and endocrinologist may help to identify subtleties. At the general examination, any evidence of dysmorphic features should be discussed with a geneticist. There are certain genetic syndromes that are associated with ambiguous genitalia, such as Smith-Lemli-Opitz and Denys-Drash. In addition, vital signs should be carefully examined, since blood pressure and fluid status can be affected by CAH.

With regard to the external genital examination, careful attention is paid to describing the length and width of the phallus, the scrotal and/or labial folds, the texture and pigmentation of the genital skin, the location of the gonads, and the presence of a urogenital sinus. Palpable or nonpalpable gonads in the scrotum or labia are particularly important physical examination findings. The stretched penile length is measured by placing a ruler at the pubic symphysis, stretching the phallus, and measuring to the tip of the glans. There are different scales used to describe the examination findings. The Prader Scale was developed in the 1950s by Dr Andrea Prader, a Swiss scientist, and was originally designed to describe female virilization in CAH; however, the use has expanded to describe the range of genital differentiation. It is a pictorial scale that ranges from stages I to V, with interpretative descriptions included (**Figure 14-4**).

Laboratory Studies

At the time of initial evaluation for DSD, a karyotype should be obtained, even if one was obtained prenatally. Performing FISH to look for X and Y markers can be conducted in a timely manner to determine



Normal ♀: Normal female external genitalia.
Stage I: Slightly virilized female, with mild clitoral hypertrophy but without labial fusion.
Stage II: Presence of posterior labial fusion with an anogenital ratio > 0.5. There is clitoromegaly and a small vaginal opening with a separate urethral opening.
Stage III: Complete fusion of the labia with a single urogenital sinus and an enlarged phallus.
Stage IV: Looks more male than female, with an empty scrotum and a phallus the size of a normal penis, with possible chordee. A single small urethral and/or vaginal opening at the base or on the shaft of the phallus would be considered hypospadias in a male but is a urogenital sinus.
Stage V: Complete male virilization, with a normally formed penis with the urethral opening at or near the tip. The scrotum is normally formed but empty.
Normal ♂: Normal male external genitalia.

Figure 14-4. Prader Scale.

the genetic sex, while awaiting full karyotype results. The most critical testing is done to rule out CAH. If there is concern for a virilized female with 46,XX and CAH, 17-OHP should be measured to look for 21-OH deficiency. This is included in newborn screening programs. This laboratory result will not be valid within the first 48 hours after birth because of the hormone surge at birth. In addition, electrolyte levels, including sodium and potassium, should be measured. Salt-wasting CAH will manifest with hyponatremia and hyperkalemia, which can be life-threatening, although in a newborn, it is unlikely to be exhibited until the second week after birth. For this reason, it is unnecessary to transfer a newborn with ambiguous genitalia immediately to an intensive care unit, since the testing can be performed safely in the setting of a well-equipped nursery.

In addition to these initial laboratory studies, a hormone profile should be conducted, and the pediatrician can work closely with the endocrinologist to choose further testing. As stated earlier, one of the most important goals of management of DSD in the newborn is to identify any life-threatening conditions, which would include checking karyotype, serum electrolyte levels, and 17-OHP levels to identify salt-wasting CAH.

Imaging

In the newborn period, the importance of imaging lies in identifying internal genitalia, primarily müllerian structures. Abdominopelvic US in the setting of ambiguous genitalia can be used to identify the presence or absence of a vagina and uterus, which are normally well visualized in the newborn period. US has poor sensitivity in defining intra-abdominal gonads. US should include the evaluation of the adrenal glands to look for hypertrophy that may be seen in CAH. Magnetic resonance imaging can be used to evaluate the patient for renal abnormalities and to better identify pelvic structures, but this may be limited by the need for anesthesia in the newborn period. It is not routinely used in the postnatal period to aid in the diagnosis or evaluation of DSD.

Determining Sex of Rearing

The initial evaluation of DSD has changed only slightly over the years, with improvements seen in molecular diagnosis, imaging, and timely laboratory data. The aspect of management that has evolved the most is the decision-making behind sex of rearing. The 2006 consensus statement and the recently revised 2015 Society for Endocrinology (United Kingdom) guidelines on the initial evaluation of an infant with suspected DSD focus most of their recommendations on the use of a multidisciplinary team, the role of support groups, and psychosocial support for the families. The decision about sex of rearing is heavily connected to the multidisciplinary team and the shared decision-making model.

Factors in Joint Decision-making

Several factors have been raised with regard to determining the sex of rearing. These include more tangible outcomes, such as appearance of external genitalia, ability to function sexually, fertility potential, gonadal malignancy potential, minimizing medical procedures, and others that are less tangible, such as anticipated gender preference of the child, psychosocial well-being, and cultural practices.

There is some evidence available to be able to guide these decisions. For newborns who are virilized 46,XX with CAH and for those who have 46,XY CAIS, most patients identify as female. Of those with PAIS and MGD, studies have shown that approximately 25% of patients have dissatisfaction with their sex of rearing. While either gender may be successfully assigned, there have been few other studies that provide a consensus on sex of rearing in patients with DSD. The decision is often made by the family and the multidisciplinary team. In complex cases in which gender assignment is unclear, some are now advocating waiting until the child identifies with a specific gender before making irreversible surgical decisions.

Ethical Considerations

As part of the multidisciplinary team, many centers advocate for a medical ethicist. This is based on the need to make decisions with transparency and in the best interests of the newborn, as well as the adult that the newborn will become, and to be respectful of parental wishes. These

are complex issues and, as emphasized throughout this chapter, they require the expertise of a multidisciplinary team and a center that is familiar with the evaluation and diagnosis of DSD.

Clinical Pearls

- The pediatrician has a key role in the initial diagnosis of ambiguous genitalia and in the evaluation of the patient to rule out life-threatening disorders.
- The pediatrician also has a role in the evaluation of delayed or absent puberty in the adolescent.
- The pediatrician is a key member of the multidisciplinary team that will be managing all aspects of the child's care throughout childhood and adolescence.
- Identification of ambiguous genitalia in the newborn is important in assessing patients for DSD.
- CAH is the most important abnormality to diagnose, as it can be life-threatening.
- It is important to include a team of specialists in the diagnosis and management of DSD from the beginning.
- Joint decision-making with the family and medical team is key in determining the sex of rearing.

Resource for Parents

- Accord Alliance. Scripts for talking with parents. http://www.accordalliance.org/dsdguidelines/htdocs/clinical/scripts.html. Accessed October 17, 2018

Suggested Readings

Lee PA, Houk CP, Ahmed SF, Hughes IA; International Consensus Conference on Intersex organized by the Lawson Wilkins Pediatric Endocrine Society and the European Society for Paediatric Endocrinology. Consensus statement on management of intersex disorders. *Pediatrics*. 2006;118(2):e488–e500

McCann-Crosby B, Sutton VR. Disorders of sexual development. *Clin Perinatol*. 2015;42(2):395–412, ix–x

Wherrett DK. Approach to the infant with a suspected disorder of sex development. *Pediatr Clin North Am*. 2015;62(4):983–999

Ahmed SF, Achermann JC, Arlt W, et al. Society for Endocrinology UK guidance on the initial evaluation of an infant or an adolescent with a suspected disorder of sex development (revised 2015). *Clin Endocrinol (Oxf)*. 2016;84(5):771–788

Diamond DY, Nithiphaisal YR. Disorders of sexual development: etiology, evaluation, and medical management. In: Wein AJ, ed. *Campbell-Walsh Urology.* Philadelphia, PA: Elsevier; 2015:3569–3497

Wiesemann C, Ude-Koeller S, Sinnecker GH, Thyen U. Ethical principles and recommendations for the medical management of differences of sex development (DSD)/intersex in children and adolescents. *Eur J Pediatr*. 2010;169(6):671–679

CHAPTER 15

Exstrophy-Epispadias Complex and Urachal Remnants

Nathan A. Brooks, MD, and Douglas W. Storm, MD, FAAP

Exstrophy-Epispadias Complex

Introduction

The exstrophy-epispadias complex (EEC) is a rare spectrum of defects that affects multiple organ systems, including the genitourinary tract, the gastrointestinal tract, the musculoskeletal system, the pelvic floor musculature, and the bony pelvis. The most common presentations of EEC are epispadias, classic bladder exstrophy (CBE), and cloacal exstrophy (CE). Epispadias is the least severe form of EEC, in which affected children present with a dorsally open urethral meatus, with mild pubic diastasis and a closed anterior abdominal wall and bladder (**Figure 15-1**).

Children with CBE present with pubic diastasis, an abdominal wall defect that exposes an open bladder, and a urethra with an epispadic opening (**Figure 15-2**). CE, which is the most severe form of CBE, has a similar presentation to CBE but also includes a portion of cecum or hindgut that separates the open hemibladders (**Figure 15-3**). CE

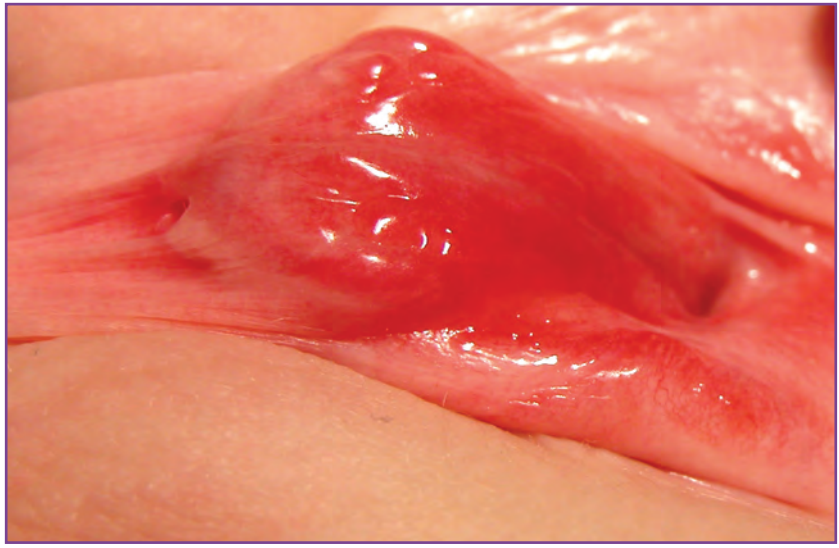


Figure 15-1. A male infant with epispadias. Note the dorsal location of the urethra and urethral meatus at the penopubic junction and the bifid appearance of the glans, as well as the penile shortening.

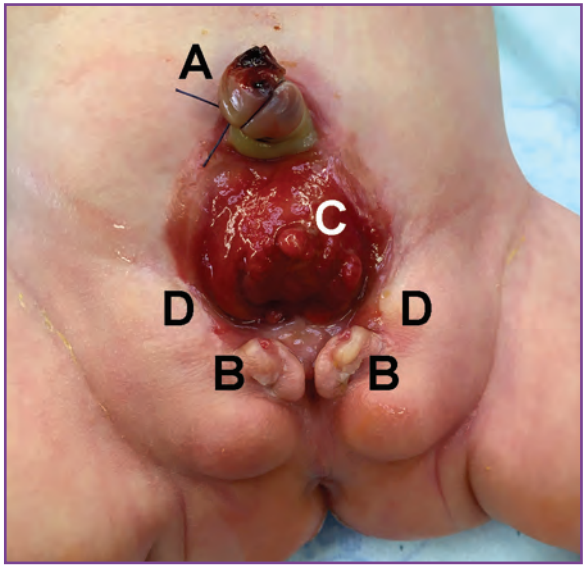


Figure 15-2. A female neonate with classic bladder exstrophy. The umbilical cord is tied with a suture (**A**) rather than a clamp. The clitoris is bifid (**B**). The bladder mucosa is apparent in the midline abdominal defect (**C**), and there is pubic diastasis (**D**).

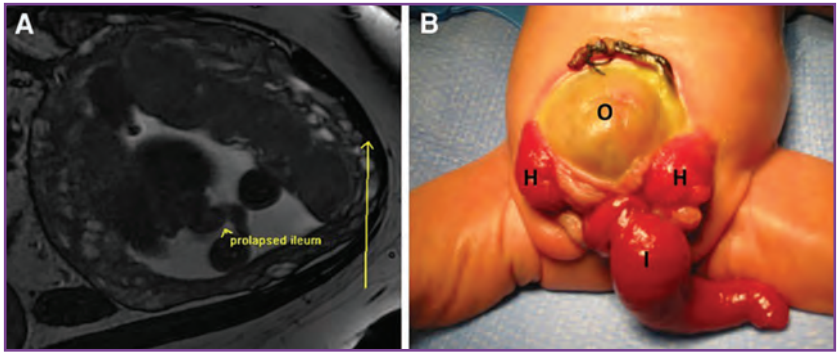


Figure 15-3. Prenatal magnetic resonance image (**A**) and postnatal photograph (**B**) in a patient with cloacal exstrophy, showing the "elephant trunk" sign that represents the intussuscepted ileum. The bladder plate is divided into hemibladders (H) by the omphalocele (O) with an "elephant trunk" ileum (I).

Reprinted with permission from Bischoff A, Calvo-Garcia MA, Baregamian N, et al. Prenatal counseling for cloaca and cloacal exstrophy—challenges faced by pediatric surgeons. *Pediatr Surg Int.* 2012;28(8):781–788.

typically also includes malformations of the gastrointestinal, musculoskeletal, and central nervous systems, also known as OEIS (*o*mphalocele, *e*xstrophy, *i*mperforate anus, and *s*pinal defects) complex.

Children with EEC typically require multiple reconstructive surgeries, intended to close the abdominal wall and bladder, realign the bony pelvis, and correct the epispadias. Often, these surgeries begin shortly after birth, with the goal of preserving renal function, achieving continence, and obtaining a normal cosmetic appearance. In this chapter, we will discuss the incidence, epidemiology, diagnosis, surgical correction, and long-term outcomes in children born with EEC.

Incidence and Epidemiology

Isolated epispadias occurs in 1 of 117,000 male births and in only 1 of every 484,000 female births. CBE is the most common presentation of EEC, occurring in approximately 1 of every 10,000 to 50,000 births. CBE affects twice as many male patients as female patients. CE is the least common EEC variant and occurs in 1 of every 200,000 births and is also twice as common in male patients.

The incidence of EEC is significantly greater in the white population. Given that EEC clusters in families, genetic factors might play a role in

the inheritance of this syndrome. Children with EEC also have a higher incidence of concomitant renal anomalies, including renal agenesis, ectopically located kidneys, renal duplication, and vesicoureteral reflux (VUR). Girls with EEC can also present with uterine and/or vaginal duplication or absence.

Pathophysiology

While the cause of EEC is not yet completely understood, it is theorized that the embryological origin of the EEC involves maldevelopment of the cloacal membrane. The cloacal membrane is composed of endoderm (the bladder and urethra are derived from endoderm) and ectoderm (derivatives include skin and neural tissue) and is located at the anterior abdominal wall. In normal development, mesenchymal ingrowth between these 2 layers results in the formation of the lower abdominal wall musculature and pelvic bones. After mesenchymal ingrowth, the urorectal septum divides the cloaca in a cranial to caudal fashion into the bladder anteriorly and the rectum posteriorly. Continued caudal descent of the urorectal septum divides the cloacal membrane into the urogenital sinus and the anal membrane (**Figure 15-4**).

It is thought that EEC occurs during the fourth gestational week, as the cloacal membrane may overdevelop, resulting in failure of mesenchymal migration. This failure in migration causes the cloacal membrane to become unstable and prone to early rupture. Failure of normal mesenchymal migration may result in malformation of the lower abdominal wall and the pelvic bones, while the timing and location of the rupture of the cloacal membrane result in the different presentations along the EEC spectrum. Epispadias develops if the rupture occurs late, resulting in nonunion at the end of the genitourinary tract. CBE results if the rupture occurs after the urorectal septum has separated the gastrointestinal tract from the genitourinary system, whereas CE results if the rupture occurs prior to this separation.

Outcome and Prognosis

Patients with EEC experience urogenital, musculoskeletal, gastrointestinal, and neuro-spinal anomalies that affect their functional outcome. In children with CBE and CE, the bladder is exposed and will need to be

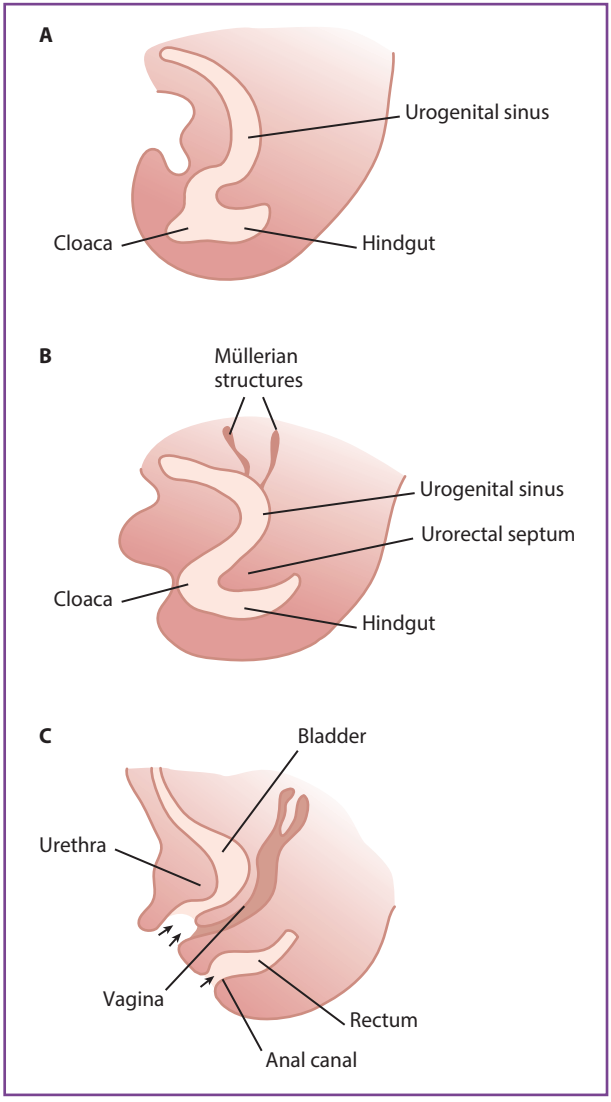


Figure 15-4. The development of the urogenital sinus. **A,** At 5 weeks of gestation, the cloaca is not separated. **B,** At 6 weeks, the cloaca is divided into the urogenital sinus and the hindgut. **C,** By 12 weeks, the 3 openings (anus, vagina, and urethra), denoted by the black arrows, are formed.

closed shortly after birth. Many of these bladders appear to be immature, and even with proper closure, the bladder may not develop as expected or achieve normal capacity. In these children, their small bladders and other associated abnormalities with their pelvic floor, bladder outlets, and sphincteric mechanisms frequently make normal voiding and urinary continence difficult to achieve. This may result in the need for further surgery to assist with bladder outlet resistance, increase bladder capacity, and even, in some cases, create a bladder substitute.

In boys with EEC, the urethra is located dorsally, and they typically have a shorter and broader phallus with dorsal chordee. In girls with EEC, the distal aspect of the dorsally placed urethra remains open, resulting in a patulous bladder neck, which may further contribute to difficulties with continence even after surgical correction of EEC. In addition, the vagina and introitus are typically displaced anteriorly, and the vagina may be shortened and stenotic. In addition, there are potentially associated müllerian anomalies, including vaginal and uterine duplication or, sometimes, complete agenesis.

Patients with EEC typically have diastasis of their pubic rami, external rotation of their anterior and posterior pelvic segments, retroversion of their acetabulum, wider sacroiliac joint angles, an inferiorly rotated pelvis, and a large sacrum. These abnormalities result in malrotation of the pelvis, causing a waddling gait. Pelvic muscular anomalies also make some female patients with EEC more prone to uterine prolapse. Patients with CBE and CE may also have an anteriorly displaced anus and anal sphincter, which, in combination with the pelvic floor abnormalities, may predispose some patients to fecal incontinence. About 7% of patients with CBE and almost all patients with CE have a spinal abnormality such as spinal dysraphism, tethered cord, and vertebral anomalies, which also necessitate surgical correction and will also contribute to gastrointestinal and genitourinary dysfunction.

Diagnosis

EEC is difficult to identify at prenatal ultrasonography (US), with only about 10% to 25% of cases being identified. Diagnosis is suggested by the absence of a fluid-filled bladder and an echogenic mass of tissue over the anterior abdominal wall at serial US imaging (**Figure 15-5**).

Figure 15-5. A, Transverse ultrasonographic (US) cross-section of the fetal pelvis shows an absent urinary bladder and 2 umbilical arteries, as well as a wide-set umbilical cord. **B,** Midsagittal US image of the fetal abdomen with a low-set umbilical insertion and anterior abdominal wall mass.

From Wolniakowski A, Szlachetka K, Thornburg LL. Prenatal diagnosis of bladder exstrophy. *J Diagn Med Sonography.* 2014;30(2):88–91.

Additional prenatal US findings suggestive of EEC include small genitalia, low-set umbilical structures, a growing abdominal mass, and a widened pubic ramus. The prolapsed ileum in CE may have an "elephant trunk" appearance at US.

Most children with EEC will receive a diagnosis at postnatal examination. A boy with epispadias will have a dorsally positioned, open urethra (see **Figure 15-1**). Children with CBE and CE will have an obvious abdominal wall defect in the midline, below the level of the umbilicus, with an open bladder plate (see **Figures 15-2** and **15-3**).

Treatment Options and Outcomes

Initial management should include ligation of the umbilical cord with a silk tie rather than an umbilical clamp, since the clamp will irritate the bladder mucosa. After this, the bladder should be covered with a nonadherent plastic wrap (**Figure 15-6**).

Gauze should never be used, as this can irritate the bladder mucosal surface and lead to polyp formation, which hinders closure and is associated with possible increased risk of adenocarcinoma of the bladder. The plastic wrap should be replaced with every diaper change. Additional evaluation should include the normal neonatal physical examination, serum studies to include complete blood cell count, renal function, electrolyte levels, abdominal radiography to evaluate the pubic diastasis and bowel gas pattern, and renal US to evaluate the patient for renal abnormalities at 24 to 48 hours after birth.

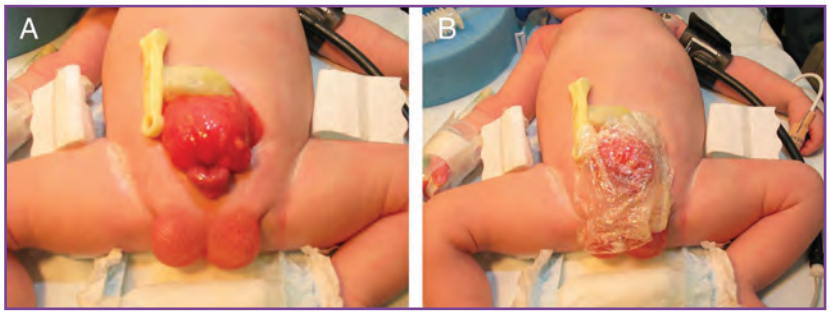


Figure 15-6. Use of plastic wrap to protect the delicate bladder mucosa in a newborn with bladder exstrophy.

Reprinted with permission from Vricella GJ, Coplen DE. Neonatal urogenital issues: evaluation and management. *NeoReviews*. 2017;18(6):e372–e385.

Patients with epispadias typically undergo surgical correction at any time after 6 months of age. If there is associated bladder neck incompetence, additional surgical procedures at a later date may be required to assist with continence.

All patients with CBE and CE will need closure of the bladder and reconstruction, with or without fixation of the pelvis. The timing of exstrophy repair is dependent on bladder size, functional capacity of the bladder, degree of polyp formation, bladder fibrosis, and preference of the surgical team.

In general, patients with CBE may be managed in a single or staged approach that includes the principles of abdominal wall closure, realignment of the bony pelvis, bladder closure, creation of a penile shaft epispadias (in preparation for later epispadias repair), correction of VUR in some patients, and bladder neck repair to establish continence.

CBE and CE closure, followed by a cystogram, frequently demonstrates VUR, as the ureters enter directly into wall of the bladder without the normal oblique course through the posterior wall of the bladder. The kidneys and ureters are assessed with renal US at lengthening intervals, as long as the imaging findings are stable or improving (degree of hydronephrosis, hydroureter, and bladder). If there is a deleterious change in the degree of hydronephrosis, prompt communication with the pediatric urologist is a must. Since almost all these patients have VUR, management after bladder closure should include antibiotic prophylaxis. After closure, the bladder capacity is anticipated to increase over time. Any patient who has recurrent urinary tract infections (UTIs) should be brought promptly to the attention of the treating urologist.

Long-term continence varies by surgical repair and definition of continence. It is important to note that in most studies, the definition of continence used for these patients is less rigorous than the "always dry" definition used in other patient populations. Those failing to achieve continence can be managed with additional procedures, including bladder augmentation with intermittent catheterization or urinary diversion (continent or incontinent). Issues with continence, the need for multiple surgeries, and the understanding that the patient is "different" from his or her peers lead to increasing psychological issues as the child ages, and many of these patients will benefit from intervention by a child psychologist.

In male patients with EES, long-term sexual function and relationships are affected, although most patients do report satisfaction with social, educational, and professional achievements. Most men are able to achieve erections. Many men are dissatisfied with the cosmetic appearance and size of the phallus. In addition, about one-third of men will have some form of anorgasmia and/or anejaculation, and only about 25% of these patients will father children. Similar to their male counterparts, CBE has a negative effect on female sexual function, though with a more varied and possibly lower effect on quality of life, as well as a decrease in fertility rates.

When to Refer

Once identified, all patients with EEC should be immediately referred to a center that specializes in EEC management and repair.

Clinical Pearls

- EEC is a rare disorder that encompasses a spectrum of disease severity.
- At most, 25% of patients with EEC will have positive screening findings at prenatal US.
- At birth, the umbilicus should be tied off *with a silk tie rather than a clamp* to avoid irritation of the exposed bladder mucosa.
- Initial management of bladder exstrophy involves covering the exposed mucosa with a plastic film covering, such as Tegaderm (3M, St Paul, MN) or Saran Wrap (S. C. Johnson & Son, Racine, WI).
- All children will need closure and reconstructive surgery.
- Urinary continence rates vary.
- All patients will have VUR; thus, management after closure should include antibiotic prophylaxis and close follow-up. Febrile UTIs should promptly be brought to the attention of the pediatric urologist.
- When transitioning care, adulthood screening should include monitoring for bladder cancer and Papanicolaou testing, with the understanding that there will be some degree of cervical displacement from the orthotopic position.

Resources for Parents

- Association for the Bladder Exstrophy Community. http://www.bladderexstrophy.com. Accessed October 17, 2018
- Urology Care Foundation. What is bladder exstrophy? http://www.urologyhealth.org/urologic-conditions/bladder-exstrophy. Accessed October 17, 2018
- National Organization for Rare Disorders. Bladder exstrophy-epispadias-cloacal exstrophy complex. https://rarediseases.org/rare-diseases/bladder-exstrophy-epispadias-cloacal-exstrophy-complex. Accessed October 17, 2018

Suggested Readings

Ebert AK, Reutter H, Ludwig M, Rösch WH. The exstrophy-epispadias complex. *Orphanet J Rare Dis*. 2009;4(1):23

Woo LL, Thomas JC, Brock JW. Cloacal exstrophy: a comprehensive review of an uncommon problem. *J Pediatr Urol*. 2010;6(2):102–111

Hankinson JC, Eldridge MA, Ostrander R, et al. Emotional and behavioral functioning in children with bladder exstrophy-epispadias complex: a developmental perspective. *J Pediatr Urol*. 2014;10(1):136–141

Murray C, Anderson D, Hurrell R. Considering the psychosocial aspects of sexual health for people with exstrophy–epispadias complex: a critical narrative review. *Sex Disabil*. 2014;32(2):175–188

Inouye BM, Tourchi A, Di Carlo HN, Young EE, Gearhart JP. Modern management of the exstrophy-epispadias complex. *Surg Res Pract*. 2014;2014:587064

Urachal Remnant

Introduction

During development, urine exits the fetus via the allantois, which will obliterate and become the urachus. Either the entire urachus or segments of the urachus can remain patent, leading to urachal abnormalities. These abnormalities can manifest with chronic or intermittent umbilical drainage or abscess, or they may remain asymptomatic for years.

Incidence and Epidemiology

A large review of radiographic imaging places the incidence rate of urachal anomalies at about 1.03%, with only 7.5% of patients presenting with symptoms. These abnormalities include patent urachus (50%), urachal cyst (30%), umbilical urachal sinus (15%), and vesicourachal diverticulum (3%–5%).

Pathophysiology

During fetal development, urine must exit the bladder to provide amniotic fluid. This is accomplished by the allantois, an extraembryonic structure derived from the yolk sac that connects to the cranioventral portion of the bladder. As the bladder moves caudally, the allantois is stretched and will eventually become an obliterated, thick, fibrous cord, also known as the *urachus.* The closed urachus will then become the median umbilical ligament. However, failure of the allantois to obliterate will lead to urachal patency. A patent urachus will occur if there is failure of the canal to obliterate and remains open between the umbilicus and the dome of the bladder. An umbilical-urachus sinus occurs if the urachus obliterates at the bladder level but remains open at the umbilicus. A vesicourachal diverticulum occurs if the urachus obliterates, except at the level of the bladder apex. A urachal cyst occurs if the urachus closes at the umbilicus and the bladder but does not obliterate between and remains fluid filled (**Figure 15-7**).

Outcome and Prognosis

Concerns regarding an untreated urachal remnant include the future potential for cancer development and the possibility of serving as the nidus for infection. In terms of malignancy potential, Ashley et al examined the medical records of 176 patients with a urachal anomaly, including 46 children and 130 adults. They found that the presentation of children and adults with urachal anomalies was different, with most children presenting with umbilical drainage and most adults presenting with hematuria and pain. Although they recommended urachal remnant excision in childhood to prevent cancer occurrence, they also commented that at their center, there is no reported evidence that a persistent urachal remnant is the cause of later cancer development. However, this study does not necessarily answer the question regarding the natural history of a pediatric urachal remnant, and no study to date,

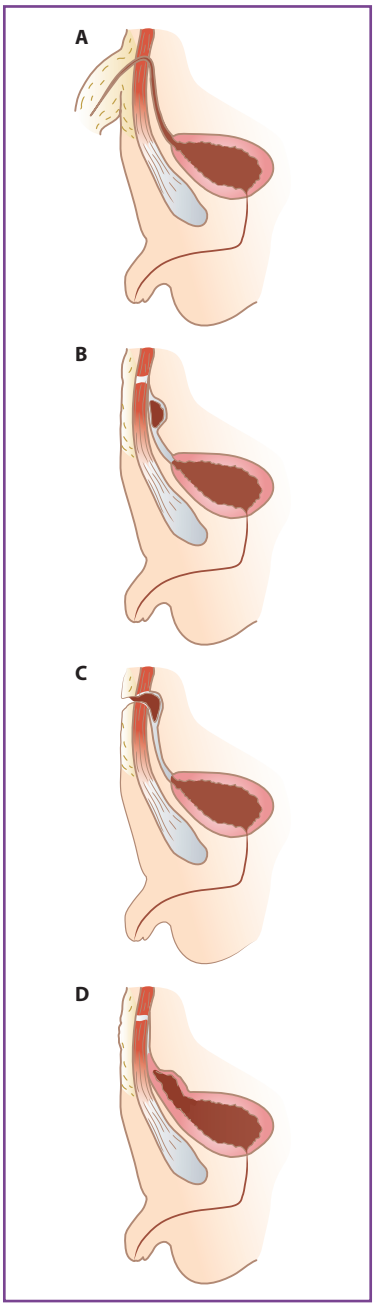


Figure 15-7. Urachal anomalies. **A,** Patent urachus. **B,** Urachal cyst. **C,** Umbilical urachal sinus. **D,** Vesicourachal diverticulum.

to our knowledge, follows up with children over time who are found to have urachal remnants to determine the risk of developing a urachal cancer in adulthood.

Urachal abnormalities may be asymptomatic or symptomatic. Symptomatic remnants may result in recurrent UTIs, stone development, or umbilical drainage or infection. If the remnant is causing symptoms, typically, surgical excision is performed. Asymptomatic remnants may be an incidental finding at bladder or pelvic US and have a high rate of spontaneous resolution by 6 months of age. In cases of persistent urachal remnants, the outcome is unclear in terms of malignancy potential and risk of future symptom development, as again, no study has followed up these remnants over an extended period, to our knowledge. Given these issues, the proper management of a child's urachal remnant, especially when its asymptomatic, remains unclear, and typically, treatment varies by surgeon.

Diagnosis and Evaluation

Patent Urachus

A patent urachus generally manifests in the neonatal period, when continuous or intermittent drainage from the umbilicus is observed, with or without delayed healing of the cord stump. A patent urachus is frequently diagnosed with voiding cystourethrography, which also helps rule out urethral obstruction as a causative factor (**Figure 15-8**).

In the case of the draining patent urachus, this may be observed, as it may spontaneously obliterate and resolve. If there is no resolution by 3 to 6 months of age, surgical excision is recommended. If the child presents because of an infection and/or abscess, the management consists of abscess drainage and antibiotics. After resolution of the infection, the patent urachus is then surgically excised.

Urachal Cyst

Urachal cysts are generally diagnosed in older children and adults. In urachal cysts, there is no communication with either the bladder or the umbilicus. However, the presenting symptom is typically intermittent drainage of the fluid-filled cyst, via either the umbilicus or the bladder. The diagnosis is confirmed with US demonstrating a cyst between the abdominal wall and the peritoneum (**Figure 15-9**). Similar to patent

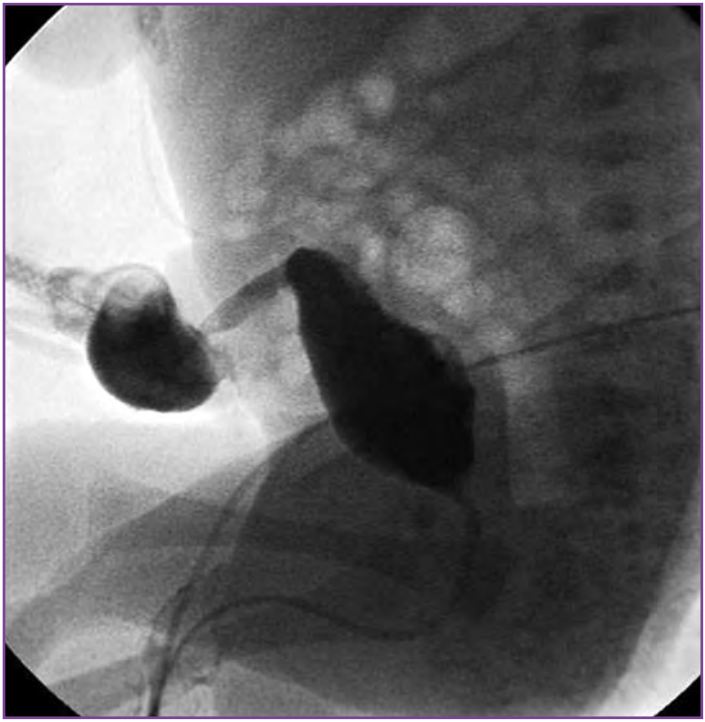


Figure 15-8. Voiding cystourethrogram demonstrates a patent urachus. Notice the filling of the urachus and extravasation via the umbilicus.

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urachus, urachal cysts can appear as an umbilical abscess or as recurrent bladder infections at presentation. Treatment also involves drainage of infection, followed by excision. Rarely, these cysts rupture into the peritoneal cavity and appear with peritonitis at presentation.

Umbilical-Urachus Sinus

The umbilical-urachus sinus represents a urachus that freely connects only with the umbilicus. The presentation is similar to both patent urachus and urachal cyst, and diagnosis is often established with US. Treatment is similar to that of urachal cyst.

Figure 15-9. Ultrasonographic image demonstrates a 1.28-cm cystic mass between the bladder and the anterior abdominal wall.

Vesicourachal Diverticulum

Vesicourachal diverticula are almost always asymptomatic and are discovered incidentally at abdominal imaging. Occasionally, stones can form inside a diverticulum, or these may result in recurrent UTIs if there is a narrow neck. In these cases, removal of the diverticulum is recommended (**Table 15-1**).

Treatment Options and Outcomes

The management and treatment approach surrounding urachal remnants remains controversial and is physician dependent. As discussed earlier, these issues stem from not having a clear understanding of the natural history of urachal remnants and their possible malignancy potential. A small urachal remnant can be viewed as a normal, physiological variant that commonly resolves by 6 months of age. However, since most persistent urachal remnants identified in older children are typically removed rather than followed up, it is unclear what would happen to the remnants over time. The fear of leaving a remnant in place stems from knowing that if identified in adults, at excision, about one-half have malignancy (usually adenocarcinoma). Therefore, given the real risk of cancer in adults, the unclear natural history of a pediatric

Table 15-1. Summary of Findings, Diagnosis, and Treatment for the Variants of Urachal Anomalies				
Variant and Percentage of Cases	**Age at Presentation**	**Presenting Symptoms**	**Diagnosis**	**Management**
Patent urachus (50%)	Neonatal period	Continuous umbilical drainage Delayed cord stump healing	VCUG	Manage infection Excision
Urachal cyst (30%)	Older children through adulthood	Intermittent umbilical drainage Hematuria	US	Manage infection Excision
Umbilical-urachal sinus (15%)	Neonatal period, early childhood	Continuous or intermittent umbilical drainage	VCUG and US	Manage infection Excision
Vesicourachal diverticulum (3%–5%)	Incidental findings	Usually asymptomatic Can present with recurrent infections	VCUG	Excision Observation

Abbreviations: US, ultrasonography; VCUG, voiding cystourethrography.

urachal remnant over time, and the limited risk and morbidity associated with surgical excision of the urachal remnant, some argue that all urachal remnants should be removed. Therefore, the patient should be referred to a urologist who is comfortable managing urachal remnants, and an informed management discussion and decision can occur.

When to Refer

Patients with urachal remnants should be referred to a specialist for discussion of management and possible surgical excision.

Clinical Pearl

The management of urachal remnants remains controversial; however, all symptomatic remnants should be treated, and patients should be referred for possible removal. The management of asymptomatic remnants involves a conversation with the patient and family regarding treatment.

Resource for Parents

Urology Care Foundation. What are urachal abnormalities? http://www.urologyhealth.org/urologic-conditions/urachal-abnormalities. Accessed October 17, 2018

Suggested Readings

Gleason JM, Bowlin PR, Bagli DJ, et al. A comprehensive review of pediatric urachal anomalies and predictive analysis for adult urachal adenocarcinoma. *J Urol.* 2015; 193(2):632–636

Ashley RA, Inman BA, Routh JC, Rohlinger AL, Husmann DA, Kramer SA. Urachal anomalies: a longitudinal study of urachal remnants in children and adults. *J Urol.* 2007;178(4 Pt 2 Suppl):1615–1618

CHAPTER 16

Urological Imaging in Pediatrics

Bhalaajee Meenakshi-Sundaram, MD, and Dominic C. Frimberger, MD

Introduction

Imaging is frequently a necessary adjunct to the history and physical examination in the complete urological evaluation and diagnosis of adult and pediatric patients. However, pediatric imaging poses a series of unique challenges not commonly faced in adult patients. It is critically important for pediatric providers to be cognizant of these issues prior to ordering pediatric imaging tests. Studies considered routine in the adult population may require specially trained technicians and even anesthesia in children. Additionally, radiation dose and pediatric-specific equipment may be required. Providers should determine the availability of equipment, the comfort level of technicians with pediatric examinations, and the ability of radiologists to interpret specific findings at their hospitals prior to ordering pediatric urological imaging. In this chapter, we describe the benefits and shortcomings of the various urological imaging modalities available, as well as the proper clinical context in which to order specific examinations.

Safety

After a practitioner determines that the imaging of the genitourinary tract is required to adequately evaluate a child's presentation, consideration should be given to the following factors prior to ordering any imaging modality: *(a)* the dose of radiation administered per study, *(b)* the need for future studies with radiation doses, *(c)* the need for general anesthesia or sedation to obtain acceptable images, and *(d)* the need for oral or intravenous (IV) contrast agents. Since precisely determining the radiation risk in individual children is potentially challenging, it is recommended that all providers utilize the "ALARA" (*a*s *l*ow *a*s *r*easonably *a*chievable) principle.

While imaging modalities with nonionizing radiation (ultrasonography [US], magnetic resonance [MR] imaging) are considered safer than the use of ionizing radiation (plain-film radiography, IV pyelography, computed tomography [CT]), it possesses clinically significant risks of its own. When MR imaging is substituted for CT, many children require sedation or general anesthesia because of the lengthy period required for image acquisition. Additionally, the use of gadolinium-based contrast material is associated with nephrogenic systemic fibrosis in children who have poor renal function. Both iodine-based contrast material used with CT and gadolinium-based contrast material used with MR imaging are associated with a small risk of allergic reaction, as well. Last, while no human data are available, it is recommended that fetal MR imaging be avoided in the first trimester, since questions remain regarding the effects on gene expression that can be caused by exposure to the magnetic field. No such concerns exist with US, which is, therefore, regarded as appropriate at any age.

Imaging modalities that are reliant on ionizing radiation are considered more harmful in children than in adults because of the increased radiosensitivity of developing tissue. Additionally, the cumulative effect of higher doses over a child's lifetime is of concern. Radiation-induced malignancies may present after a prolonged period from the initial exposure. Variations in patient size and age, as well as imaging technique, must be taken into account prior to ordering imaging with ionizing radiation in children. Typically, the ionizing radiation modality with the highest radiation dose—CT—is not required for common pediatric urological presentations. Plain-film radiography is associated with a lower dose and is considered safe when used judiciously.

Prior to choosing an imaging study, the following questions should be answered:

- Will the study answer the clinical question?
- Will the results alter patient management?
- Is there a previous study that has already answered the current question?
- Is there a safer alternative, or one without nonionizing radiation?

Prenatal Imaging

The use of prenatal imaging has become widespread, since multiple congenital abnormalities can be diagnosed with prenatal US. Within pediatric urology, US provides information on the presence and quality of the renal parenchyma, the position within the retroperitoneum, and the presence of a reference level of amniotic fluid. Conditions such as hydronephrosis, renal cystic disease, and solid masses may be detected with antenatal US. The normal appearance of the fetal upper urinary tract should consist of renal parenchyma that is isoechoic with the liver, discrete corticomedullary differentiation, the absence of cortical cysts, and the absence of fluid or dilation of the collecting system and ureters. By contrast, the fetal bladder may demonstrate variable fluid volume as a result of typical bladder cycling.

Dilation of the collecting system of the kidney and parenchymal cysts are common findings at prenatal US. Dilation of the collecting system is commonly referred to as *hydronephrosis.* It is graded on a scale of I to IV, on the basis of the appearance at US. A more detailed discussion about prenatal hydronephrosis may be found in Chapter 9, Congenital Hydronephrosis.

Ultrasonography

US is the first-line study for investigating suspected renal or scrotal abnormalities in children. It is relatively cheap and does not use ionizing radiation. However, it is highly operator dependent. Hydroureteronephrosis should always be evaluated when the bladder is empty to determine the full extent of upper-tract (kidney and ureter) dilation and to distinguish between hydronephrosis from an obstruction at the ureterovesical junction and bladder outlet obstruction. The average newborn kidney is approximately 4.5 cm in length in a

longitudinal view. US is particularly useful in assessing kidney anatomy, size and shape, corticomedullary differentiation, presence of dilation, and presence of solid masses (**Figures 16-1** and **16-2**).

US is also the imaging of choice for suspected testicular or scrotal pathologic processes. Genital imaging is typically used in the case of the acutely painful or enlarged scrotum, testicular or paratesticular masses, undescended testes, and ambiguous genitalia. However, it should be noted that US should not be used in the routine evaluation of cryptorchid testes. Instead, it may be reserved for cases in which the patient is obese or unable to tolerate the examination. In such cases, the presence of an inguinal testis at US may guide the surgical approach. In cases of the acutely painful or swollen scrotum or testicle, the differential diagnosis includes testicular torsion (**Figure 16-3**), epididymo-orchitis, hernia, and torsion of the appendix testis.

Torsion is characterized by the absence of flow to the testis in question, while epididymo-orchitis is characterized by hypervascularity. While scrotal US can be valuable in the diagnosis of both, it is not 100% accurate in ruling out torsion, and surgical exploration for suspected testicular torsion should not be delayed if the physical examination findings

Figure 16-1. Renal ultrasonography shows normal corticomedullary differentiation.

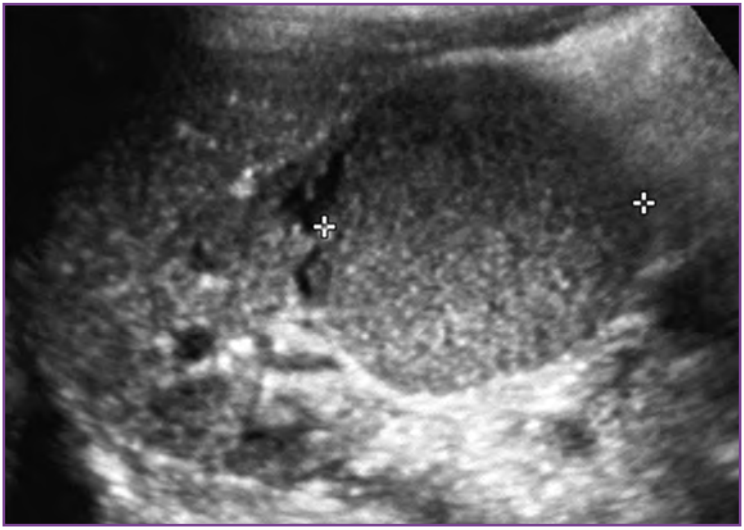

Figure 16-2. Ultrasonography shows nephroblastoma (Wilms tumor) of the kidney with replacement of normal renal architecture.

Reprinted with permission from Martin AD, Pohl HG. Pediatric urogenital imaging. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology*. 11th ed. Philadelphia, PA: Elsevier; 2016:2909–2925.

and the history are consistent with torsion. In other words, US should be performed to confirm the clinical impression that the patient does not have testicular torsion.

Scrotal US is also used in the diagnosis of pediatric testicular and paratesticular masses. The most common prepubertal tumor is a mature teratoma, characterized by areas of solid, cystic, and calcified components. Yolk sac tumor is the most common malignant tumor. It is characterized by a well-vascularized, solid mass. The images in **Figure 16-4** demonstrate the features of a yolk sac tumor as a well-localized mass.

Voiding Cystourethrography

Voiding cystourethrography (VCUG) is a study that provides information on the lower urinary tract (ie, the bladder and urethra). Indications for VCUG include febrile urinary tract infections (UTIs) or high-grade hydronephrosis. The study should not be performed in the setting of an active UTI. The technique for the study is described as follows:

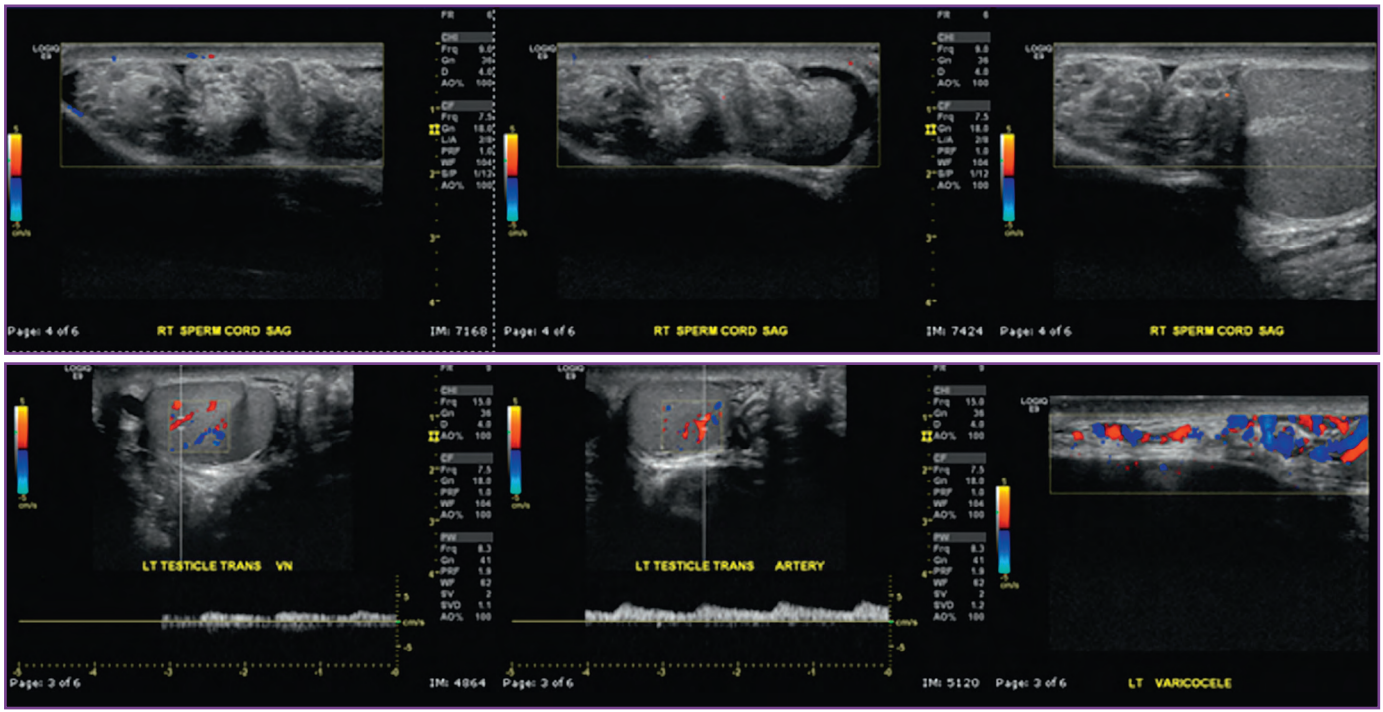

Figure 16-3. Absence of flow to the right testis and epididymis at Doppler ultrasonography, with normal flow to the left testis, consistent with right testicular torsion.

Reprinted with permission from Martin AD, Pohl HG. Pediatric urogenital imaging. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology*. 11th ed. Philadelphia, PA: Elsevier; 2016:2909–2925.

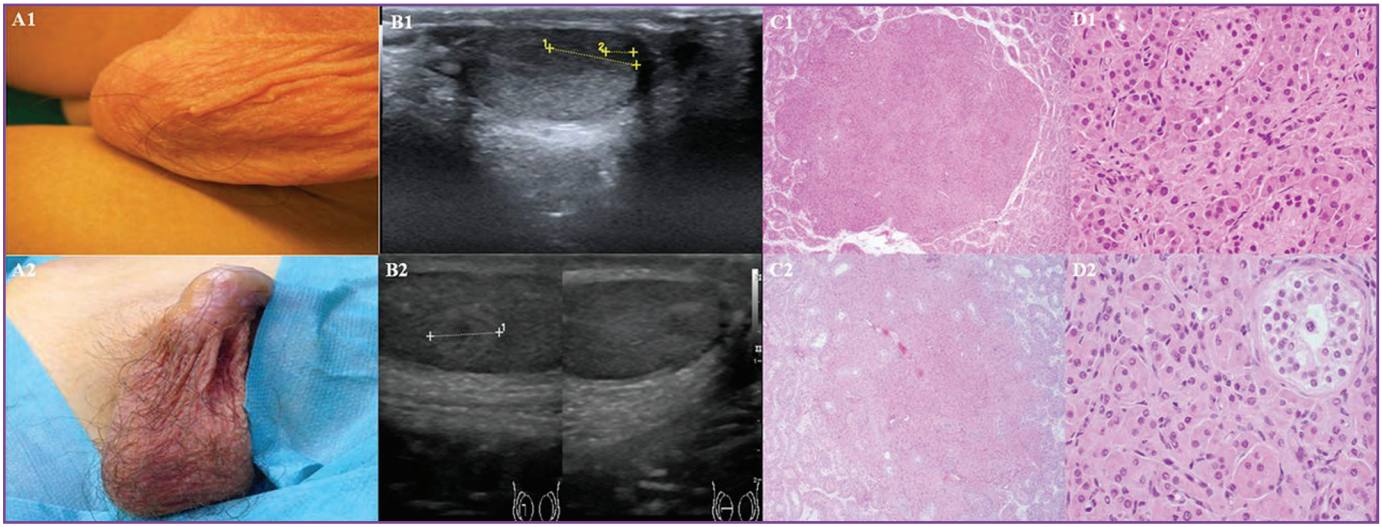

Figure 16-4. The upper row depicts a yolk sac tumor in patient 1. The lower row shows a yolk sac tumor in patient 2. Image A on both rows illustrate the clinical findings. **A1,** Patient 1 has monolateral, curled pubic hair on the left testis. **A2,** Patient 2 has monolateral testicular hair, adult type. Image **B** on both rows shows testicular ultrasonography of a hypoechoic testicular mass. Images **C** and **D** show histologic findings (hematoxylin-eosin stain; original magnification, ×4 on **C** and ×40 on **D**). Note the neoplastic cells with abundant eosinophilic cytoplasm and the distinct cell borders arranged in nests and cords.

Reprinted with permission from Mameli C, Selvaggio G, Cerini C, et al. Atypical Leydig cell tumor in children: report of 2 cases. *Pediatrics.* 2016;138(5):e20160151.

A small feeding tube (typically 6 or 8 French) is passed into the bladder per the urethra. A scout image is then obtained. Contrast material is instilled with fluoroscopic observation, under gravity. Serial radiographs of the pelvis and abdomen are obtained. Views of the kidneys and an oblique view of the male urethra are obtained once voiding has started. Ensuring that this is a voiding study is important because 20% of reflux occurs only with voiding, and voiding images help define the urethral anatomy.

VCUG is an excellent study for defining the anatomy of the bladder and urethra, as well as providing information with regard to bladder emptying. Lower-tract abnormalities detectable at VCUG include vesicoureteral reflux (VUR), bladder trabeculation, ureteroceles, diverticula, posterior urethral valves, and urethral strictures (**Figure 16-5**).

With regard to the upper tract, VCUG is the study of choice for detecting VUR. *VUR* refers to the retrograde flow of urine into the ureters

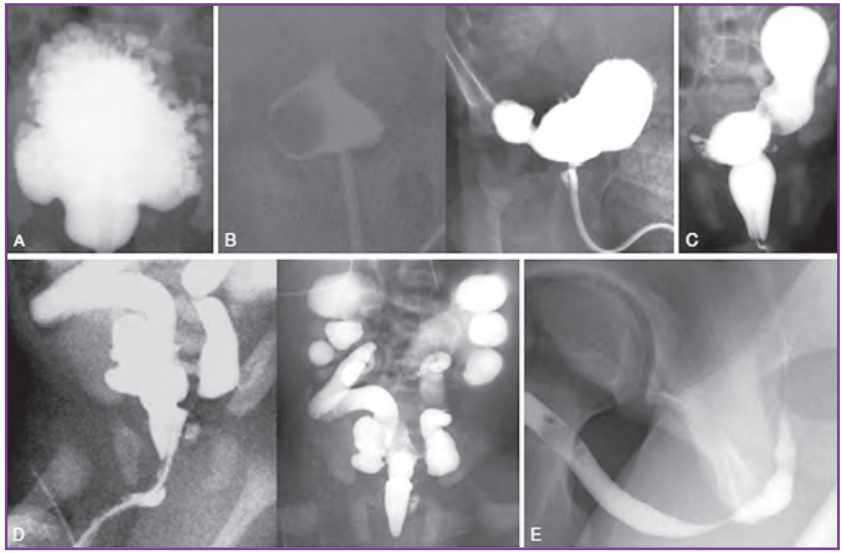

Figure 16-5. A, Heavily trabeculated bladder. **B,** Intravesical ureterocele. **C,** Large bladder diverticulum. **D,** Posterior urethral valves with vesicoureteral reflux. **E,** Bulbar urethral stricture.

Reprinted with permission from Martin AD, Pohl HG. Pediatric urogenital imaging. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 11th ed. Philadelphia, PA: Elsevier; 2016:2909–2925.

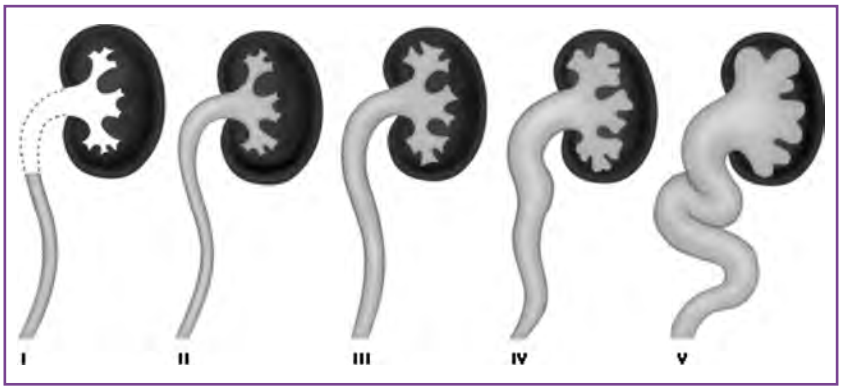

Figure 16-6. Grades of vesicoureteral reflux. Grade I indicates reflux into the nondilated ureter. Grade II indicates reflux into the renal pelvis and calyces without dilatation. Grade III denotes mild to moderate dilatation of the ureter, renal pelvis, and calyces, with minimal blunting of the fornices. Grade IV indicates dilation of the renal pelvis and calyces, with moderate ureteral tortuosity. Grade V indicates gross dilatation of the ureter, pelvis, and calyces; ureteral tortuosity; and loss of papillary impressions.

Reprinted with permission from Keren R, Carpenter MA, Hoberman A, et al. Rationale and design issues of the Randomized Intervention for Children With Vesicoureteral Reflux (RIVUR) study. *Pediatrics.* 2008;122(Suppl 5):S240–S250.

and kidneys during voiding. It is the result of an inadequate valve mechanism at the ureterovesical junction and is graded as shown in **Figure 16-6.**

Computed Tomography

With advances in US and MR imaging, the need for CT in pediatric patients has dwindled. It has little role in the detection and management of hydronephrosis, as it offers little advantage over US. Similarly, CT has a limited role in the management of children with nephrolithiasis when compared with adults. However, there are select circumstances in which it is very valuable, such as in upper- and lower-tract trauma. In blunt abdominal trauma, CT with IV contrast material can be used to detect renal and ureteral injuries. In pelvic trauma with suspicion for bladder injury, CT cystography is performed with retrograde filling of the bladder. Complete bladder filling is required to assess the patient for smaller injuries and leaks. CT is superior to plain cystography because of 3-dimensional views and an improved ability to distinguish between intraperitoneal and extraperitoneal bladder ruptures—2 conditions

that are managed differently. Ultimately, CT should be used sparingly in children and has very specific applications. If a provider does elect to use CT in a child's diagnostic evaluation, the ALARA principle should be followed.

Magnetic Resonance Imaging

MR imaging has gained traction within pediatric urology in recent years because of its ability to provide high-spatial-resolution anatomic detail of the upper and lower urinary tracts, without exposing patients to ionizing radiation. While it is not as useful as other studies in the setting of infection, stones, or trauma, it is very useful in characterizing complex congenital abnormalities when US cannot provide sufficient detail.

For lower-tract evaluation, MR imaging can be used as an adjunct to US in disorders of sexual differentiation. However, US, genitography, and direct visualization typically provide sufficient anatomic and structural details for preoperative planning in patients with disorders of sexual differentiation. The sensitivity and specificity for identification of internal structures, including the gonads and müllerian strictures, may only be marginally better.

In the evaluation of the upper tract, MR imaging has emerged as a useful alternative to IV urography or nuclear medicine scintigraphy in the assessment of the anatomy and function of kidneys. Information regarding function and anatomic detail can be obtained in one study, without exposing children to radiation. One particular condition in which MR imaging is particularly useful is the identification of an ectopic ureter in a patient with a duplicated ureter (**Figure 16-7**).

In such cases, MR imaging assists with the diagnosis, as well as with surgical planning. In some centers, MR urography has become increasingly prevalent in the diagnosis and surgical planning of ureteropelvic junction obstruction. While this is a novel application of MR imaging, it should be noted that the availability, costs, and need for anesthesia preclude this approach in many patients.

Nuclear Medicine

Nuclear scintigraphy is used for assessing the function and drainage of the kidneys. It typically provides information only on the function of the upper tracts and does not provide anatomic detail. Nuclear scans are

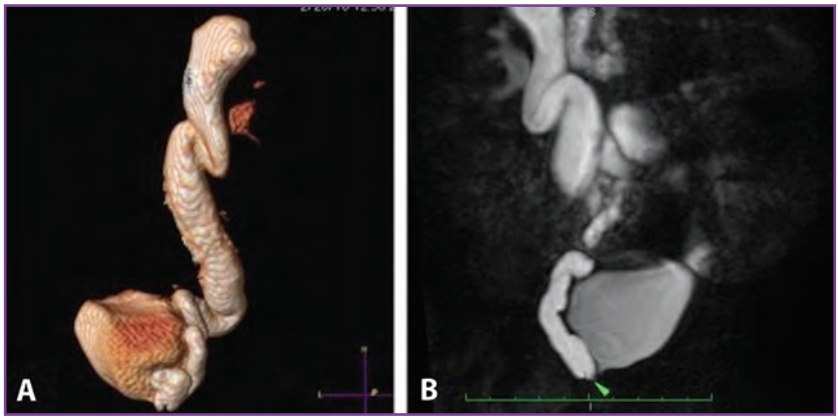

Figure 16-7. A, Three-dimensional magnetic resonance (MR) reconstruction and **B,** sagittal MR images demonstrate ectopic insertion of the ureter.

From Gaweesh TY, Etaby AN, El-Noueam KI, Hamimi AH, Youssef ME. Static fluid magnetic resonance urography in evaluation of ureteral ectopia: experience in 10 pediatric cases. *Alexandria J Med.* 2013;49(1):49–55. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (https://creativecommons.org/licenses/by-nc-nd/3.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

divided into 2 categories, cortical and diuretic. For both types of studies, placement of an IV catheter is required for administration of the radiotracer. In diuretic nuclear renal scans, a Foley catheter is often required to completely drain the bladder to prevent bladder distention, which may result in an artificial appearance of obstruction of the upper tracts.

Renal Cortical Scintigraphy

Renal cortical scintigraphy is performed by using technetium 99m (^{99m}Tc) dimercaptosuccinic acid (DMSA). It relies on uptake of DMSA by the proximal tubular cells of the nephron, a process dependent on renal blood flow. Based on the timing of the study relative to the UTI, it is useful in diagnosing acute pyelonephritis and renal scarring due to VUR. When performed in the setting of an episode of pyelonephritis, the DMSA scan is likely to demonstrate areas of photopenia that correspond to inflammation (**Figure 16-8**). This inflammation is typically transient and resolves within 6 months. However, in cases in which postinfectious scarring is present, persistent photopenia with loss of renal cortical contour will be noted (**Figure 16-9**). For pediatric

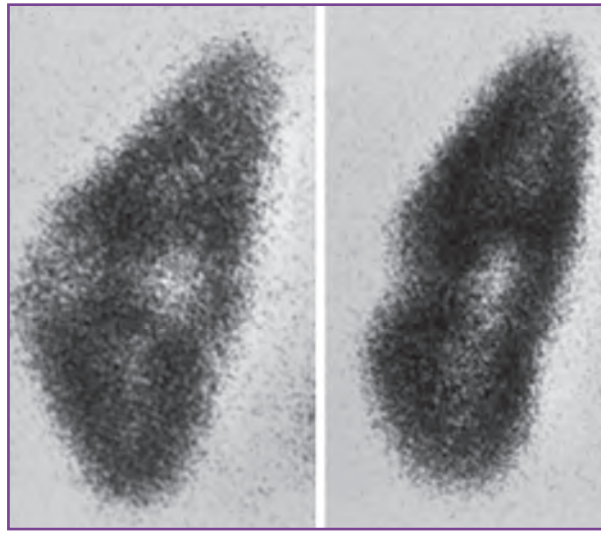

Figure 16-8. Renal scan shows areas of photopenia along the periphery that correspond to inflammation. Renal contour is preserved.

Reprinted with permission from Martin AD, Pohl HG. Pediatric urogenital imaging. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology*. 11th ed. Philadelphia, PA: Elsevier; 2016:2909–2925.

urologists, the presence of scarring is particularly important, as it may prompt surgical intervention for correction of reflux, while patients in whom scarring is absent may continue to be observed.

Diuretic Scintigraphy

Diuretic scintigraphy is performed by using either ^{99m}Tc diethylenetriamine pentaacetic acid or ^{99m}Tc mertiatide (MAG_3). MAG_3 is more commonly used because of its availability. Diuretic scintigraphy and renography are used to differentiate between obstructive and nonobstructive etiologic origins for hydronephrosis. A strict protocol should be used to ensure reproducible results. To perform an adequate study, the child should be well hydrated, and the bladder should be drained. Inadequate hydration may artificially portray obstruction by demonstrating a slow uptake curve and corresponding slow drainage. Although catheter placement is not routinely required, if placed, a catheter does remove any element of obstruction at the level of the bladder, providing a true measurement of upper-tract drainage.

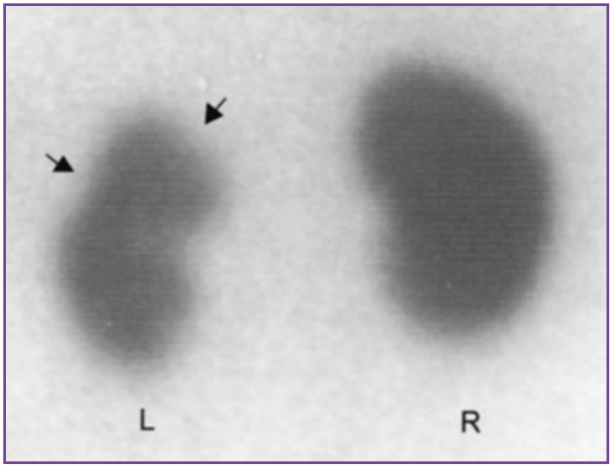

Figure 16-9. Technetium 99m dimercaptosuccinic acid renal scan shows a normal posterior projection of the right kidney but defects in the left kidney (marked by arrows) on the lateral aspect of the cortex and at the upper pole. These represent areas of renal scarring.

Reprinted with permission from Decter RM. Vesicoureteral reflux. *Pediatr Rev.* 2001;22(6):205–210.

Prior to the study, as noted previously, an IV catheter and a Foley catheter should be placed. The radiotracer should then be administered, and images are collected during the uptake phase. During this phase, which occurs from 1 to 3 minutes after radiotracer administration, the differential function of the 2 kidneys may be assessed. At maximal dilation of the collecting system (10 and 20 minutes after the start of the study), IV furosemide (1 mg/kg) should be administered to prompt drainage from the kidney, thereby initiating the drainage phase. It is during this phase that ureteropelvic junction or ureterovesical junction obstructions can be distinguished from physiological stasis.

Management decisions are made on the basis of renal function. In contrast to adults, there are no established drainage times for children. A child with prolonged drainage but stable and symmetrical function may be observed. Indications for surgery to correct obstruction include diminished function, recurrent infections, or the formation of stones due to stasis. The MAG_3 scan of a patient with ureteropelvic junction obstruction and diminished renal function is shown in **Figure 16-10**.

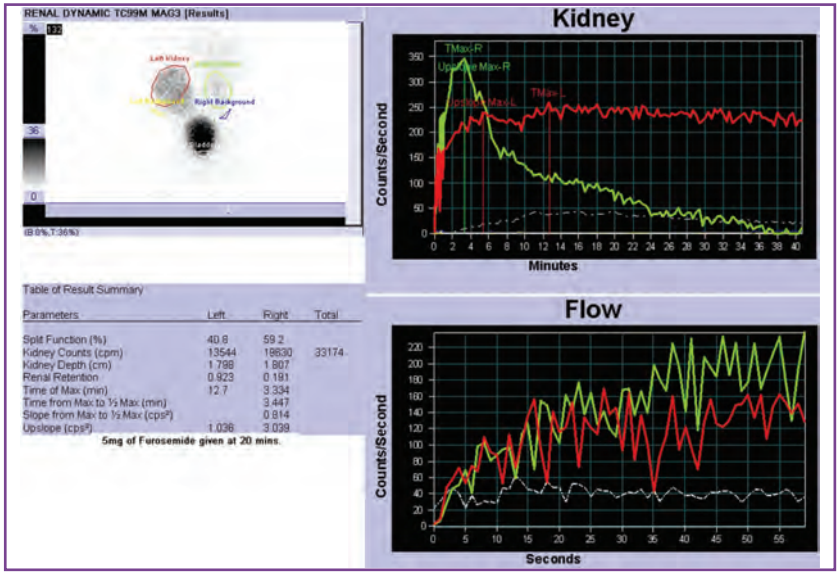

Figure 16-10. Technetium 99m mertiatide furosemide renal scan demonstrates high-grade ureteropelvic junction obstruction, with left kidney function of 41% and right kidney function of 59%. The left renograph also demonstrates a prolonged drainage curve (red line), indicating poor drainage. On the basis of these findings, the patient was treated with pyeloplasty.

Clinical Pearls

- The ALARA (*a*s *l*ow *a*s *r*easonably *a*chievable) principle should be followed when considering the use of imaging with ionizing radiation in children.
- A normal renal US finding in the presence of acute pyelonephritis does not preclude VUR. VCUG is required to rule out VUR.
- US in cryptorchid testes should be reserved for children with obesity in whom physical examination is difficult.
- CT should only be used in select circumstances in children.
- MR imaging is useful in children and does not involve the use of ionizing radiation, but sedation or general anesthesia may be required.
- Renal function is more important than drainage time at diuretic renography, in making the decision to perform surgery.

- It is important for providers to determine the available equipment, the comfort level of technicians with examinations, and the ability of radiologists to interpret specific findings at their institutions prior to ordering urological imaging.
- If safer or nonionizing alternatives are available, providers should exhaust these alternatives prior to ordering images that are reliant on the use of ionizing radiation.

References

1. Don S, Macdougall R, Strauss K, et al. Image gently campaign back to basics initiative: ten steps to help manage radiation dose in pediatric digital radiography. *AJR Am J Roentgenol*. 2013;200(5):W431–W436
2. Thomsen HS, Marckmann P, Logager VB. Nephrogenic systemic fibrosis (NSF): a late adverse reaction to some of the gadolinium based contrast agents. *Cancer Imaging*. 2007;7:130–137
3. Arthurs OJ, Bjørkum AA. Safety in pediatric imaging: an update. *Acta Radiol*. 2013; 54(9):983–990
4. Dias T, Sairam S, Kumarasiri S. Ultrasound diagnosis of fetal renal abnormalities. *Best Pract Res Clin Obstet Gynaecol*. 2014;28(3):403–415
5. Senasi R, Raghavan A. Imaging of the urinary system. *Pediatric Urology Book*. http://www.pediatricurologybook.com/Imaging_urinary_tract.html. Accessed October 18, 2018
6. American Urological Association. Fifteen things physicians and patients should question. http://www.choosingwisely.org/societies/american-urological-association. Updated May 26, 2017. Accessed October 18, 2018
7. Martin AD, Pohl HG. Pediatric urogenital imaging. In: Wein AJ, Kavoussi LR, Partin AW, Peters CA, eds. *Campbell-Walsh Urology.* 11th ed. Philadelphia, PA: Elsevier; 2016:2909–2925
8. Gaweesh TY, Etaby AN, El-Noueam KI, Hamimi AH, Youssef ME. Static fluid magnetic resonance urography in evaluation of ureteral ectopia: experience in 10 pediatric cases. *Alexandria J Med.* 2013;49(1):49–55
9. Biswas K, Kapoor A, Karak AK, et al. Imaging in intersex disorders. *J Pediatr Endocrinol Metab*. 2004;17(6):841–845
10. Majd M, Rushton HG. Renal cortical scintigraphy in the diagnosis of acute pyelonephritis. *Semin Nucl Med*. 1992;22(2):98–111
11. Shulkin BL, Mandell GA, Cooper JA, et al. Procedure guideline for diuretic renography in children 3.0. *J Nucl Med Technol*. 2008;36(3):162–168

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Pediatric Urology
for Primary Care

Editors
Saul P. Greenfield, MD, FAAP, FACS
Christopher S. Cooper, MD, FAAP, FACS

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